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THE LOCALIZATION OF THE MENTAL FACULTIES IN THE LEFT PREFRONTAL LOBE.

By Charles Phelps, M.D.,
SURGEON TO BELLEVUE AND ST. VINCENT'S HOSPITALS, NEW YORK CITY.

In order to ascertain with the greatest possible certainty whether the law which seemed to have been established by my own observations, connecting symptoms of mental disorder or default exclusively with left prefrontal lesion, was absolute, still larger groups of cases with limited lesions were gathered without discrimination from such sources as were available, and subjected to analysis.

These were divided into three classes: 1, atrophies; 2, pistol-shot wounds; 3, abscesses and tumors.

First: Cerebral atrophies form a smaller class than either of the others, and are very often unsuited to the study of cerebral localization by reason of associated congenital idiocy. Idiots, lunatics, and epileptics suffer from general cerebral disturbances which make it usually impossible to define the pathological relations of lesions of special areas. If progressive mental decadence begins at some period subsequent to birth, and hemiatrophy is found to exist, it might be a legitimate inference that they are directly related. It is better, however, to limit the field in which it is sought to establish the relation between a normal or an abnormal mental condition and a cerebral atrophy to less complicated cases.

I have found only twelve cases reported in comparatively recent years, including two in the series of traumatisms recorded by me heretofore. There are probably others which I have failed to discover, or which are noted in Continental journals, which I have not consulted. The number is so small that they may be reproduced here in more or less detail.

CASE I.[1] *General atrophy.*—Patient, aged fourteen years. "Mind a miserable wreck." The brain was shrivelled, but particularly in front and on the upper and lateral part of the left hemisphere; the surface was irregular, as though elevated; and rose to various heights according to the degree of atrophy.

CASE II.[2] *Left hemiatrophy.*—Idiot girl, aged seven years; hemiplegia from infancy; indicated early all the signs of imperfect mental development; speech very defective; communicated mainly by gestures and inarticulate sounds; imbecility progressive; "became more and more like an unclean beast;" remarkable atrophy of the right side of the body.

Necropsy. "Right hemisphere of cerebrum apparently quite healthy; color of gray matter was the usual light red, and convolutions were natural." Left hemisphere much smaller; whole hemisphere soft and fluctuating like a bladder, on account of the ventricular fluid; gray matter very pale and yellow; convolutions much thinned; arachnoid membrane much thickened on left side, and considerable subarachnoid fluid. Atrophy of the right cerebellar lobe and of the right side of the spinal cord. Skull much thickened on the left side.

CASE III.[3] *Left hemiatrophy.*—Patient, aged seven years; quite well till within seven weeks; illness began with convulsions; great mental decadence; could understand at times, but had no power of speech; did not know his own bed; ate his own feces; walked actively, but dragged his limbs a little; right side of body atrophied and flabby; left hospital in nine weeks, returned five months later, and died from a burn four months afterward.

Necropsy. Left hemisphere smaller in all its dimensions; right hemisphere quite normal.

CASE IV.[4] *Left hemiatrophy.*—Patient, aged forty-five years; mental condition not stated.

CASE V.[5] *Atrophy of both frontal lobes.*—Patient, aged seventy-three years; under observation for five years; during first three years showed some signs of mental alienation; speech entirely ceased; asked for nothing either by eye or gesture; food put in his hand, even, was not carried to his mouth; did not recognize his companions or the bed in which he slept, or know when he was cold; "finally lost all sentiment of spontaneity of will;" no hemiplegia.

Necropsy. Atrophy of both frontal lobes, involving first, second, third, and ascending frontal convolutions; also ascending parietal convolutions and paracentral lobules.

CASE VI.[6] *Left hemiatrophy.*—Patient, aged fifty-five years; "there was a deficiency of intelligence."

Necropsy. Left hemisphere weighed three and one-quarter ounces less than the right; convolutions softened to depth of one-fourth inch.

CASE VII.[7] *Left hemiatrophy.*—Patient at age of two years was feeble-minded, and at about that time became paralyzed; at ten years of age he became epileptic.

[1] Barlow. Lancet, 1849, vol. i. p. 92.
[2] J. L. C. Schroeder and Van Der Kolk. A Case of Atrophy, etc. London, 1861.
[3] Jones. London Medical Times and Gazette, 1874, vol. i. p. 371.
[4] Boyer. Bull. Soc. Anat., 1877, p. 609.
[5] Baraduc. Bull. Soc. Anat., 1876, p. 277.
[6] Boyd. Med. Chir. Trans., vol. xxix. p. 18.
[7] Spiller. Journal of Nervous and Mental Disease, 1898, p. 1.

Necropsy. The entire left lobe was notably diminished in size; the prefrontal lobe was well developed. The motor fibres of the left hemisphere were totally destroyed, yet he was able to walk without a crutch. The left pyramidal fibres were entirely destroyed.

CASE VIII.[1] *Left hemiatrophy.*—Patient, a child, aged eleven months, died from diarrhœa after five days' observation at the New York Foundling Asylum. Was exceedingly restless and prone to beat its head against the side of the crib.

Necropsy. A pad of fibrous tissue well supplied with bloodvessels, closely adherent to the dura mater, and separable from the pia mater only by tearing, covered the left half of the brain; marked atrophy of nearly the whole left hemisphere; tip of frontal, the occipital, and lower portion of temporal lobe normal; throughout the shrunken portion the convolutions were small, hard, and of a yellow wax-like color. The middle cerebral artery was apparently intact and pervious. The fibrous pad was considered to be secondary to the atrophy.

CASES IX. and X.—Atrophy of both frontal lobes and of the left frontal lobe, respectively, are detailed in the previous series of traumatisms.

CASE XI.[2] *Right hemiatrophy.*—Patient was a woman, aged thirty years, mentally and physically well till the close of her fourth year, when she became epileptic. At school she was able to learn fairly well. Subsequently she manifested an ill-will to children. The irritability and violence which led to her being placed in an asylum arose in part from her epilepsy and in part from her being a subject of ridicule to young children from her uncouth appearance. "After admission to the asylum she employed her time in reading the Bible and complaining about her illness." She had no aphasia and no hemiplegia. She died from phthisis pulmonalis.

Necropsy. The convolutions of the left hemisphere were normal in size and appearance. The right hemisphere was greatly atrophied, both as regarded size generally and as to the frontal, parietal, and occipital convolutions. The right superior middle and inferior frontal convolutions were present, but were of only one-third the size of those of the opposite hemisphere. The ascending frontal convolutions could not be defined with any accuracy. The corresponding portions of the centrum ovale were also atrophied. "The small side of the pons corresponded with the left or atrophied side of the cerebellum, while the small sideof the medulla was the right, corresponding with the atrophied side of the cerebrum."

CASE XII.[3] *Right hemiatrophy.*—The patient was for three years previous to his death under the observation of Dr. Pearce Bailey. He had left hemiplegia, with rigid contractures of the arm and leg, and scarcely any other symptoms; only a little subjective numbness; no objective anæsthesia; no loss of special sense; and no loss of control of sphincters.

In contrast with the pronounced physical symptoms, pointing to an extensive lesion of the right half of the brain, was the absence of disturbances referable to the psychic faculties. Speech was perfectly

[1] Bovaird. Med. Record, 1899, vol. ii. p. 762.
[2] Howden. Journ. Ment. Sci., 1875, p. 288.
[3] Bailey. THE AMERICAN JOURNAL OF THE MEDICAL SCIENCES, 1899, vol. cxvii. p. 321.

normal; reading was not interfered with; memory was apparently unaffected.

"I never noticed in my frequent conversations with him during the three years, nor was there ever reported to me by the house staff or attendants, anything to indicate that the man's character or mental capacity had been affected in any way by the cerebral affection. He was courteous, intelligent, and patient; he was cheerful and attentive, and his power of attention was very good; he read the papers attentively, liked to talk politics, and was interested in the affairs of the hospital. He was singularly free from fits of depression, emotional excitement, irritability, apathy, or of any other of the manifestations of abnormal mental states. He was cleanly, and required such care only as his physical infirmities rendered necessary."

Necropsy. "Dura mater moderately thickened over anterior part of the right hemisphere; beneath it in this region was a cyst in the meshes of the pia mater, six inches in diameter. The left hemisphere was normal in size and in configuration of the convolutions. The right hemisphere was greatly shrunken. That portion of it posterior to the fissure of Rolando was atrophied in the individual convolutions, but the convolutions retained their natural topography. The region anterior to this fissure, comprising all the frontal lobe except that part lying to the inner side of the olfactory tract, was occupied by a yellowish-white semi-translucent œdematous tissue overlying a soft mass as a membrane. Its surface was very uneven, presenting elevations and depressions in such wise as to suggest diminutive convolutions. On section it was found to be dirty white in color, fibrous, and somewhat more resistant than brain tissue, and showing no brain matter.

"Thus the macroscopical appearance of the right hemisphere presented posterior to the fissure centralis a slight atrophy of the brain substance, while anteriorly to it nearly the whole frontal region was represented by a shapeless mass. There was no atrophy of the cerebellar hemispheres, but there was of the right basal ganglia and of the right half of the pons and medulla."

Microscopical examination. The membrane covering the mass was thickened pia mater; the mass itself was connective tissue, cells, and fibres, and a very friable amorphous matter which contained blood pigment. There were no traces of ganglion cells new-growth as such.

There are three cases of right hemiatrophy quoted by Van Der Kolk, which, like the two just described at length, afford striking evidence of the independence of the intellectual faculties of anatomical substrata in the right cerebral hemisphere.

These were: Andral's case; traumatism confined to right hemisphere; "pia mater formed a cyst in which no traces of cerebral matter remained;" floor formed by optic thalamus, corpus striatum and parts on a level; "yet he had a good education, had a good memory, good address, and exhibited as much intelligence as most men."

Thiaudiere's case: Same mental condition as in that of Andral; nothing remained of the right hemisphere but atrophied corpus striatum and optic thalamus.

Gall's case: Clergyman preached and catechised three days before his death; half of the right hemisphere completely softened and changed into a yellow granular substance.

Three of the preceding cases are not convincing; two as instances of atrophy involving both frontal lobes, and one as the history of an idiotic subject. The twelve others afford substantial evidence that the control of the mental faculties resides exclusively in the left hemisphere.

Second: Pistol-shot wounds are especially well calculated to exemplify differences in symptoms, as the right or left lobe is the seat of lesion, since they are injuries in which the lesion is often strictly localized. The whole number of cases reported from English and American sources during the years 1879 to 1895, inclusive, is probably not more than 150, of which it has been possible to collate for the present purpose 110; 58 of this number involved the frontal lobes; 26 of these were limited to the right lobe, and 24 to the left lobe; eight included both lobes. The cases which terminated in recovery, and on that account probably deemed most worthy of record, were in large proportion; and in them the situation of the lesion was made certain by the use of the probe, by operation for the removal of the ball, or by the appearance of brain matter at the surface. Not one of the 26 cases in which the cerebral wound was confined to the right side presented at any time any symptom of mental or emotional disturbance aside from the stupor or delirium which is characteristic of general contusion.

In 32 cases the ball traversed the left frontal lobe, in 8 of which there was no means of determining the mental condition, the primary loss of consciousness having been permanent or the general symptoms entirely unnoted. In 13 of those remaining, manifestations of mental derangement were distinctly evident. In several of the others the mental condition was not specifically mentioned, and the histories were otherwise deficient. There are still a limited number of cases in which with a wound of the left lobe the mental faculties were said to have been unimpaired; some of these cases are stated to have exhibited some form or degree of aphasia, and in nearly or quite all of them the lesion was of the posterior part of the lobe.

This series of cases, so far as the histories are complete and intelligible, fully indicates that intellectual and emotional derangement are symptomatic, not only of lesion of the left frontal lobe, but also of its anterior and central portions.

Third: Cerebral abscesses and tumors, like pistol-shot lacerations, are often limited to a single lobe, and therefore like them are well suited to a study of the relation which symptoms bear to the site of injury. A collection of cases of this character involving the frontal lobes which I have made is wholly confirmatory of the conclusions which have been deduced from the examination of cases of traumatic origin. It

comprises all the cases, both those reported in full and those condensed from the transactions of societies in the leading English and American journals from 1891 to 1900, inclusive. It also includes the earlier cases instanced by Ferrier to demonstrate the absence of motor function in the frontal region. Out of 607 limited lesions of the nature specified, 137 were of the frontal lobes, 21 of which were not further specialized; and in 18 others the mental conditions were not mentioned; leaving 98 cases for analysis; 51 of these involved lesion of the left, and 34 of the right lobe, and 13 of both lobes. The lesions in all cases were verified by post-mortem examination.

The cases in which lesion was limited to the left lobe were 51 in number; of these, 46 presented symptoms of mental default or disorder, and 5, it was said, did not. The affirmative cases are too numerous for description in detail, but some generalizations will serve to indicate the character of their symptoms. In many cases which were briefly stated the mental condition is noted simply as one of "mental failure," "dementia," or "decadence," or of "psychical changes." In others, stupor or stupidity, apathy, hebetude, silliness, loss of power of comprehension, loss of interest in affairs, general or special changes in character, delusions, irritability, incoherence, loss of memory, refusal to speak, various disturbances of speech, and still other individualizations of mental disorder, singly or in combination, are variously specified. As might naturally be expected, the observation made for direct traumatisms, that subcortical disintegrations or extensive cortical lacerations were usually followed by mental default rather than by mental aberration, has an application to the lesions now under consideration. Tumors or abscesses centrally developed which attained large size were very characteristically accompanied by stupor, hebetude, or apathy too profound to admit the manifestation of more positive psychical changes. If the lesion were of smaller extent at the time the history of the case began, a greater number of mental symptoms was likely to be developed in its progress. The loss of the power of attention, which Ferrier regarded as the essential result of his removal of the prefrontal lobes in certain of the lower animals, and which some writers have insisted upon as characteristic of prefrontal lesion in the human subject, was not a distinctive symptom of the acute traumatisms which have been described, and it does not seem to have been recognized as such in these cases of more chronic development. It was undoubtedly often noticeable in the progress of the cases which I have personally observed, but only as an incident of general conditions of hebetude, apathy, indifference, or progressive dementia, not as a primary defect. Another symptom which has been regarded as a specific indication of frontal lesion is a loss of control of the rectal and vesical sphincters. This diagnostic inference is true only in certain cases. It then implies

a lack of mental self-control resulting from deficient will, or a mental impairment by which the exercise of reason and judgment is prevented or suspended. Lack of sphincteric control from such mental deficiency was illustrated in the case of tumor, Case I., recorded heretofore.[1] In that instance the attendants noted in the beginning the patient's evident first impulse to get up and go to the closet, and then his momentary hesitancy before he urinated in the bed. It is, however, quite as frequent as an indication of laceration of any other part of the brain as of this, and is diagnostic of the nature rather than the seat of the lesion.

In an enumeration of symptoms indicative of mental disorder or default dependent upon left frontal lesion, delirium and loss of consciousness in whatever degree must be excluded. These conditions attend general cerebral lesions, such as hyperæmia and œdema, or the cortical inflammation which is a factor in arachnitis. They occur in cases involving distinctive left frontal injury, but the always possible or probable existence of a concomitant general lesion prevents their acceptance as localizing symptoms. They are not only not characteristic of limited lesion, but are more pronounced in its absence, and directly proportionate to the extent of the general circulatory disturbance. If the cerebral contusion is slight it will not occasion delirium or a recognizable loss of consciousness; if it is well marked some degree of delirium, or some loss of consciousness, is inevitable.

If the cases which have been cited have been correctly interpreted, other forms of mental disturbance or mental default do not occur without an additional and specific lesion of the left frontal lobe. Delirium is a mental disorder, and as such, it would seem, should be referable to the same frontal area. It would not be unreasonable to suppose that it depends upon that part of the general lesion which implicates centres through which the mind is controlled, just as the irregular movements or imaginary sights and sounds may depend upon implication of the motor or of the visual and auditory centres.

Consciousness has been variously defined, but all definitions heretofore have involved an assertion of the activity of the mental faculties. It is, in fact, ordinarily manifested by the exercise of these faculties, and the persistency of mental activity while consciousness remains, even when all other cerebral functions have been suspended, is so nearly constant that its absolute constancy has been assumed, and consciousness held to be another name for the mind itself. There are reasons for believing that consciousness may be differently construed; that it is no more than a mere subjective recognition or sense of existence—a passive condition of being which simply permits the exercise not only

[1] THE AMERICAN JOURNAL OF THE MEDICAL SCIENCES, April, 1902, p. 570.

of the mental faculties, but of all the functions of the cerebral system. In a state of entire unconsciousness these functions while, it may be, preserving their integrity are in abeyance; if the loss of consciousness be incomplete, one or all of them may be roused to limited action. The exercise of the intellectual faculties, like the exhibition of feelings or emotions, the production of voluntary motion, or the appreciation of tactile or special sensation, is an accident, not an essential attribute, of this state of simple existence. The dictum of Hughlings Jackson, that "will, reason, memory, emotions, are artificially distinguished aspects of one thing,"[1] remains true; but that "one thing" is a state of mental energy rather than a "state of consciousness." This conception of consciousness is sustained by three considerations:

1. Mental activity may exist when consciousness is abolished. This happens in dreaming, in the unconscious condition of general anæsthesia, and in the hypnotic or somnambulic state.

2. Consciousness may exist when the mind is wholly inactive. This proposition is based in part upon introspection, or, to speak more exactly, upon retrospection, since phenomena cannot be studied at the exact instant of their occurrence. (Sully.) The same power of directing the attention inward to the phenomena of mind can be directed equally to a study of consciousness devoid of mental phenomena. It is the experience of many persons that there are occasions between sleeping and waking when the oblivion of slumber has given way to an indefinable sense of existence, void of feeling of pleasure or of pain, or of perception of time or place, which precedes the resumption of thought. This form of evidence, rejected by Comte, is recognized in modern psychological investigation, and will appeal to the judgment of different investigators according to their degree of confidence in their own and in other people's accuracy of subjective analysis of feeling as well as of mental processes. There are also certain observations of pathic conditions which confirm the reality of such a conscious state of mental vacuity. The inception of returning consciousness after the heavy sleep which sometimes marks the passage of the crisis in typhoid or other fever has been described by patients as being without thought or feeling, or, again, as being characterized by feeling without thought or emotion. In some cases of cerebral traumatism consciousness is in part regained, as shown by the feces and by responses to cerebral stimulation, when no signs of intelligence can be obtained. Localized cutaneous irritations will produce corresponding localized movements in parts controlled by the inferior cerebral sensorimotor centres, and pupillary contraction will follow stimulation of the visual area. The case of the child detailed heretofore[2] is strongly illustrative of the condition of

[1] "Evolution and Dissolution of the Nervous System," British Medical Journal, 1884, p. 704.
[2] THE AMERICAN JOURNAL OF THE MEDICAL SCIENCES, April, 1902, p. 575.

consciousness without the slightest evidence of mental life, which in this instance was prolonged for a number of days.

If, then, consciousness and mind may exist independently of each other, they certainly are not convertible terms.

3. The traumatic structural alterations by which consciousness is impaired or destroyed, and by which mental action is disordered, are different in character and extent. Mental disorder or default results from a limited lesion of a specialized area, which, in fatal cases at least, is usually destructive; consciousness is destroyed in greater or lesser degree by a general lesion which inhibits the cerebral nutritive processes, and is effective according to its extent, without reference to the region involved. This fact—that consciousness is not lost except when a considerable part of the brain has been functionally destroyed by inanition of its cells, without reference to region, while each differentiated cerebral function may be destroyed by a lesion of a very limited but recognized area—is pathological proof that the conclusion reached on other grounds, that consciousness is independent of mental activity, is correct.

In 5 out of the 51 cases of left frontal tumor or abscess, as in 2 others in which both lobes were implicated, it is stated that the mind was unaffected. These were:

CASE I.[1]—Traumatic. "Patient cured; preserved his reason; could walk and talk."

CASE II.[2]—Tumor. Epilepsy for ten years; patient "intelligent."

CASE III.[3]—Tumor of cortex. "The mental condition was normal."

CASE IV.[4]—Traumatic abscess. Slight wound over left orbit; on the sixth day patient was "dull and heavy," and on the seventh day was trephined; ten months later, "boy was in perfect health; no mental impairment."

CASE V.[5]—Traumatic. Ramrod driven quite through the skull from just above left orbit, emerging over left motor area of brain; no brain matter followed; probe passed into cranial cavity; temperature normal; right arm clumsy; neither temperature nor paralysis increased; on second and third days bits of brain were extruded not to exceed altogether the bulk of a filbert.

CASE VI.[6]—Traumatic. Gunshot wound transversely through middle of both lobes; "no mental symptoms; died from encephalitis some months later."

CASE VII.[7]—Lesion of both lobes. Patient "retained his senses and intelligence until fatal encephalitis set in."

Not one of the cases affords evidence to justify a conclusion that the mental condition remained normal. In 6 of them no detail of history

[1] Morrin. Quoted by Ferrier from Pitres. Localization of Cerebral Disease.
[2] Batten and Collins. Brain, 1898, p. 291.
[3] Beevor. Brain, 1898, p. 291.
[4] Southam. Brit. Med. Journ., 1891, vol. i. p. 1015.
[5] Barritt. Lancet, 1891, vol. i. p. 18.
[6] Trousseau. Gaz. Hebd., 1864.
[7] Fayer. Quoted by Ferrier. Localization of Cerebral Disease.

is given—nothing but the mere assertion of the writer that the patient "preserved his reason," "retained his intelligence," or "had no mental symptoms," or "no mental impairment." Two of the patients whose intellect remained above reproach died of chronic "encephalitis," and another was an epileptic fourteen years. The lesion in the seventh case, the fifth of the series, if a wound of the brain at all, was evidently, from the history given, no more than a scratch upon its surface; 4 of the cases are of traumatic origin, and are not properly referable to any one of the groups which have been collated for examination. They have been cited only in order that every known case of alleged infraction of the law that left prefrontal lesion occasions mental disturbance should be given consideration.

The 11 cases of conjoined lesion of both frontal lobes, presenting psychopathic symptoms, have in that regard nothing to distinguish them from similar cases in which the left lobe alone is involved.

The number of tumors and abscesses confined to the right frontal lobe is somewhat smaller than the number of those of the opposite lobe.

There were in all 34 cases, 24 of which, it is distinctly stated, suffered from no form of mental impairment; 10 cases are described as attended by symptoms of mental disorder or default. They were:

CASE I.[1]—Abscess. Death in two days after development of symptoms, from rupture into right lateral ventricle and asphyxia; aphasia was the only symptom mentioned.

Aside from the existence of a possible functional anomaly, the occurrence of aphasia demonstrated the extension of disease to the left lobe.

CASE II.[2]—Tumor. "Occupied whole extent of right frontal lobe; left motor area appeared quite healthy; decussation of pyramids normal. A convulsion was the first symptom noted; this was followed later by complete right hemiplegia; the patient was mentally very dull."

The occurrence of right hemiplegia indicates that the left hemisphere suffered from the general increase of intracerebral pressure, which, at the same time, obscured the mental faculties.

CASE III.[3]—Cyst. Situated in right frontal lobe, below the level of the corpus callosum. Motor disturbances of the left side and left face; patient became drowsy and apathetic.

Apathy is recognizable as a psychopathic symptom only when unattended by drowsiness. It seems in this instance to have been caused by an increase of intracerebral pressure following operation.

CASE IV.[4]—Abscess. Destroyed nearly the whole substance of the lower and anterior two-thirds of the right frontal lobe, and contained about three ounces of pus. A second and smaller abscess situated beneath ascending frontal and ascending parietal convolutions. Purulent bronchiectasis of lower two-thirds of right lung. Pain in right frontal region; convulsive seizures of left side of face; mental hebetude

[1] Mangan. Brit. Med. Journ., 1896, vol. ii. p. 1037.
[2] Sharkey. Brain, 1898, p. 291.
[3] Sharkey. Ibid.
[4] Eskridge. New York Medical Journal, 1895, vol. ii. p. 168.

on the seventeenth day; left hemiplegia; semi-consciousness; coma; operation; trephination over right motor area; one to one and one-half ounces of pus evacuated from smaller abscess; larger abscess not discovered.

Hebetude, semi-consciousness, and coma evidently resulted from gradually increasing intracranial pressure.

CASE V.[1]—Syphilitic tumor situated in posterior part of the first and second right frontal convolutions. Epileptiform convulsion, followed by left hemiplegia; "mental condition very much impaired." Patient recovered from all symptoms under antisyphilitic treatment, and again on their recurrence. Later, died in a convulsion.

Toxæmic origin of mental symptoms demonstrated by their disappearance under specific treatment.

CASE VI.[2]—Syphilitic tumor situated in right frontal subcortex. Patient maniacal and incoherent, with delusions.

Mental condition the probable result of syphilitic toxæmia.

CASE VII.[3]—Syphilitic gummata in centre of right frontal lobe and old syphilitic meningitis. Duration of disease five years; after three years gait became ataxic; extreme dementia; muscular tremor of tongue, lips, face, and fingers; knee-jerk exaggerated; severe convulsions occurring three months before death; diagnosis of paresis made.

Symptoms were properly attributed by the writer (Clark) to pressure from products of chronic meningitis.

CASE VIII.[4]—Sarcoma of right frontal lobe following trauma. Mental decadence and loss of memory; epilepsy for twelve years.

As site of the original injury is unknown the anatomical basis of the early mental symptoms cannot be determined.

CASE IX.[5]—Glioma and cyst of right frontal lobe, involving middle of first convolution and subjacent white substance; intracranial pressure greatly increased; convolutions flattened and sulci effaced. "Marked change in mental condition; silly expression; at times irritable, obstinate, and passionate; at other times depressed and stupid; memory markedly impaired; delusions of suspicion; severe general epileptiform convulsions."

The excessive intracerebral pressure was evident in the flattening of the convolutions and effacement of the sulci. It seems probable, however, from the nature of the symptoms as well as from the great amount of pressure, that other structural changes, not mentioned in the history, had taken place.

CASE X.[6]—Traumatic meningitis and abscess. Abscess occupied greater part of right frontal lobe; "right hemisphere enlarged at expense of right temporal and left frontal lobe." Apathetic on the third day; stupor later; operation; trephination in both frontal regions disclosing arachnitis, with much serous effusion and pial hemorrhage; recovery four months later; some loss of memory and occasional attacks of stupidity or indifference to surroundings, with bulging of both trephine openings; patient intelligent, but reasoning power slow. On reopening the wound on the right side eight ounces of pus were evacuated.

[1] Bramwell. Brain, 1899, p. 1.
[2] Beadles. Lancet, 1896, vol. i. p. 102.
[3] Clark. Journal of Nervous and Mental Disease, 1895, p. 273.
[4] Clarke. Brain, 1898, p. 291.
[5] Bramwell. Brain, 1899, p. 1.
[6] McCosh. Medical News, 1896, p. 42.

Both the primary and the secondary mental impairment, like the symptoms in the previous case, are explained by the greatly increased intracranial pressure.

The reasons assigned for believing that in each of the foregoing cases such evidences of mental derangement or default as existed were to be accounted for on other grounds than the right frontal lesion is scarcely open to question. In some of them the clinical history proved the extension of disease to the left side; in others there was an admitted toxæmia, which is known to derange or suppress the functions of the cerebral nerve centres; and in many the increase of intracerebral pressure was sufficient to produce whatever symptoms of abnormal mental condition were manifest.

The influence of increased intracranial or intracerebral pressure has been generally recognized as the constant source of confusion in estimating the pathological value of cerebral lesion. Ferrier[1] has remarked the difficulty of distinguishing between "causation and co-existence" and "the continual source of doubt which exists as to whether effects are the direct consequences of the lesion or merely the expression of general functional derangements," and Charcot[2] has pointed out "the necessity of accepting with extreme caution cases of tumor compressing the cerebral convolutions, since the effects of pressure may be felt at a distance from the seat of the lesion." This is true not only for tumors and abscesses, but for limited traumatisms attended by marked general contusions. It is in either case the secondary vascular derangements which produce pathic conditions so like those of the essential lesion as to render them indistinguishable from each other. It is, therefore, the comparatively limited and single traumatisms, or the idiopathic lesions which are merely destructive or are insufficient in size to occasion more than localized circulatory disturbance, which must form the basis for cerebral localization. The acceptance of this proposition involves the exclusion not only of cases of right frontal lesion opposed to the contention of an exclusive control of the mental faculties on the left side, but of many left frontal lesions which sustain it. Of the 57 cases of left frontal lesions in the series under consideration a considerable number were undoubtedly in this category, but by far the greater number were so limited in size as to make it possible to legitimately connect them with the symptoms of mental derangement exhibited.

A collection of cases was made by Starr,[3] some years ago, with direct reference to their bearing upon the question of a centre or centres of control in this region for the mental faculties; but no intimation was

[1] Localization of Cerebral Disease, London, 1878, p. 2.
[2] Rev. Mens., 1877, vol. 1. p. 6.
[3] M. A. Starr. THE AMERICAN JOURNAL OF THE MEDICAL SCIENCES, 1884, p. 366.

given by him of any closer specialization of such a centre in either lobe, to the exclusion of the other. Ten of the histories which he cites make no mention of the mental condition; 4, which involved the left frontal lobe, note symptoms of mental derangement, and in 5 of the 9 limited to the right frontal the mental condition was stated to be normal; 2 of the right frontal lesions, an abscess and a sarcoma, were of long duration, and toward the end of life the patient became in the one case morose, and in the other incoherent—conditions common to all exhausting diseases at their close, and neither of them infrequent, as general nutritive changes in the brain increase. The 2 cases remaining, both reported by Mills, were cases of syphilitic tumor; the first invaded the gyrus fornicatus and corpus callosum, and thrust the hemispheres apart anteriorly; the second extended into the parietal lobe; and in both mental decadence was unquestionable. It may be said of these cases that they are to be excluded from consideration in the study of localization on two grounds, previously stated: (1) Their size and their implication of contiguous parts, causing disturbance of general cerebral circulation and function; (2) the concurrent syphilitic toxæmia, which might equally with the local lesion have been the cause of the cerebral symptoms present.

The mass of clinical evidence which has been here presented entirely justifies the expressed belief of Hughlings Jackson that centres of control exist in the forepart of the brain which form the substrata of the higher mental operations. Further, it equally justifies the writer's contention that these higher centres of control are resident in the left, to the exclusion of the right prefrontal lobe. The mental default, decadence, or aberration; the apathy, imbecility, delusions, changes in character, and lapses of memory—some one or more of which in some degree marked every instance of left prefrontal lesion—and their absence as specific symptoms in practically every instance of right prefrontal lesion, are facts for which no other explanation seems adequate. If the facts as reported in some exceptional instance hereafter should seem to be irreconcilable with this localization it should be borne in mind that on the one hand symptoms as well as lesions are often negligently observed, and that on the other their significance often fails of recognition. The positive evidence afforded by such cases as have been cited in which both *ante-mortem* and *post-mortem* conditions have been determined is not to be invalidated on the mere report of a few scattered cases made by possibly untrained observers, or supported only by histories deficient in the record of essential facts.

There may be other cases, like those of Mills previously cited, which, on account of the known competency of the observer, are to be more seriously regarded. Even such cases, should they be found to exist, and, unlike the Mills cases, inexplicable by other conditions, are not to

be accepted as necessarily fatal to the doctrine of a specially localized control of the intellectual faculties. It is always possible that vital points may have been omitted from the clinical record or from the notes of post-mortem examination in the history of a case reported by any observer, however competent or eminent, and it is not at all improbable in case the observations were made many years before the questions were raised which gave these omissions their vital importance.

If in the future it should be proven beyond cavil that instances of special mental default or derangement have followed upon lesion limited to the right prefrontal region, or that lesion similarly involving the left side has been unattended by mental disorder, such facts would still be consistent with the localization in the left lobe of a centre of control for mental operations. It will be remembered that cases of hemiplegia have been reported in which the lesion was of the same side, and that in each an explanation was found in the anomalous absence of decussating fibres in the medulla oblongata. Such an anomalous condition is by no means infrequent. Trousseau's case of left hemiplegia with aphasia, upon the strength of which he denied the truth of Broca's discovery, may have been of the same character; though, in the absence of necropsy, the existence of independent lesions in the left frontal and right parietal lobes is an equal possibility. Many years ago twenty-six instances of absence of the corpus callosum had been collated. Functional anomalies are also of more or less frequent occurrence. Control of the speech faculty resident in the third right frontal convolution of right-handed persons has been several times reported.

Barton's,[1] Bromwell's,[2] and Collier's[3] cases are all comparatively recent. Luy's case, in which an aphasic patient had begun to reacquire the faculty of speech, and in which the right frontal lobe was found disproportionately developed, is of the same nature. It is conceivable that in any case an apparently contradictory pathological relation may be reconciled to an already established general law by the discovery of structural or functional anomalies. Certainly, no case in which mental disorder might be found to occur in connection with exclusive right prefrontal lesion should be given weight until after an exhaustive search for other pathological alterations has been supplemented by equally careful examination of anatomical structure.

The question finally arises as to the import of a case in which symptoms may be supposed to have been carefully observed and post-mortem examination, both of lesions and of anatomical structure, to have been minutely made, and in which mental default or derangement had been found to have had no other physical basis than right prefrontal lesion. In such case would it necessarily follow that the localization of the

[1] British Medical Journal, July 28, 1877.
[2] Brain, 1898, p. 343.
[3] Lancet, March 28, 1899.

mental faculties in the left prefrontal lobe is erroneous? The answer lies, in part, in a reference to certain facts and considerations connected with the practically unquestioned localization of the faculty of articulate speech.

1. The faculty of articulate speech is itself an intellectual faculty. This proposition is based upon the fact that aphasia is a mental and not a motor default. In aphemia or agraphia the muscles involved are neither paralyzed nor paretic, and their power of co-ordination is retained except for movements of articulation alone. It is the loss of a single memory—of one out of many memories. Objects are remembered in all their relations, but the muscular movements necessary for their symbolic expression are forgotten.

2. The intellectual faculties collectively will hold no closer relation to their physical basis than does any one of them individually. "Reason, judgment, and memory are the mental endowments chiefly concerned in the manifestations of intelligence" (Dalton). The measure of proof required for the localization of reason and judgment should not be different from that for memory, nor for memory, in general, different from that required for the one of its specializations which is essential to the function of articulate speech.

3. The localization of a centre of control for articulate speech in the third left frontal convolution is no longer questioned, yet in essential instances lesion of that part in right-handed persons has failed to cause aphasia, as in the cases of Barton, Bramwell, and Collier, to which reference has been made. Again, in left-handed persons this centre is normally located on the right side. It is also true that in destructive lesion of the speech centre on the left side speech may not be altogether lost, or, as in Luy's case, may be in some degree resumed. In all these cases functional power normally resident in the left side of the brain has been assumed by the right side, either as a congenital functional anomaly or as a compensating phenomenon.

Ferrier has pointed out that a compensating interchange of function by different centres is anatomically impossible, and, further, that motor activity exists after destruction of cortical motor centres only in so far as it is primarily or secondarily automatic and organized in the lowest centres; but he recognized the fact that the sound hemisphere after destruction of its fellow "is capable of influencing in greater or lesser degree movements of the limbs and other parts on both sides of the body."[1] Hughlings Jackson believes that "every centre represents all parts, but each centre represents some one very specially,"[2] and this should apply to the higher as well as to the middle

[1] Functions of the Brain, p. 367.
[2] Evolution and Dissolution of the Nervous System.

centres. It is, perhaps, a not altogether unreasonable assumption that in case of the mind centres, which have no corresponding lower or more automatic centres, the intellectual activities specially represented in one frontal lobe should be more largely represented in the opposite side than are voluntary movements. Whatever importance may be attached to such surmises, the essential fact remains that the control of articulate speech may in certain instances reside in the right instead of the left frontal lobe.

If, then, the localization of all the intellectual faculties is to be governed by the same laws; and one of these faculties—that of articulate speech—concededly localized in the left frontal lobe, may exceptionally be controlled by a centre in the right lobe; it will follow that exceptional instances of mental default occasioned by destructive lesion of the right lobe will not militate against the evidence of control of the intellectual faculties by a centre or centres in the left prefrontal lobe afforded by the almost if not quite invariable production of intellectual disorder or default by lesion of that region, and of that region alone.

It is somewhat remarkable that the same considerations which have led to a more or less general belief that centres controlling psychical manifestations reside in the anterior regions of the brain should not have led to their further localization on its left side. Bouillaud was astonished that his predecessors had not made the "easy discovery," as he termed it, that the centre of speech was located anteriorly in the brain; yet he himself equally failed to discover that his own observations demonstrated that it was also limited to the left side. So many recent cases have been recorded which show a direct dependence of well-marked mental disorder upon left frontal lesion, and so many other cases in which, with extensive right frontal lesion, the mental faculties had been unimpaired, that it would seem at least a suspicion of the truth should have been aroused. It must be admitted, however, that a complete demonstration of the existence of centres controlling mental functions and their localization in a limited cerebral area is essentially difficult. The insufficiency and uncertainty of functional analysis, which Broca declared to be the greatest obstacle to the settlement of disputed questions in cerebral localization, have for many faculties ceased to be factors in the problem; but they still remain the chief difficulty encountered in establishing the relation between the mental faculties and a physical basis. Paralysis or convulsive movements, whenever the result of pathic processes or experimentally produced, and losses of special sense, can be estimated at their exact value; the loss of muscular power or of sight or hearing are comparable with an unvarying standard of normal function, and their appreciation is unaffected by the subjectivity of the observer. In some cases of mental disorder the characteristic conditions are so emphasized that their

significance cannot be mistaken; many such have been detailed. In other instances, far more numerous, the mental condition is dominated by a general cerebral lesion, and all localizing symptoms are lost in delirium or coma. In other cases, more numerous still, in which less evident though positive derangements of the complicated mechanism of the mind exist, not only the want of general standards of comparison, but ignorance of the mental idiosyncrasies and limitations of the patient, and often the very brief opportunity afforded for the study of psychical disturbances before the intercurrence of delirium or access of final coma, render conclusions uncertain. The temperament and methods of the observer himself, also, will be an unknown quantity to be reckoned with. In an estimate of mental integrity or impairment, where nice distinctions are to be made, perhaps no two observers will hold to quite the same opinions. The varying extent and character of their clinical training, their different habits of observation, variations in their general acuteness of perception, justness of inference, and accuracy of statement, their comparative familiarity with the study of psychical disturbances—all lead to more or less divergent views of the same case.

In the great majority of instances, therefore—those in which frontal lesion is trivial or even of moderate extent, and in which psychical symptoms are not clearly distinctive—it is only exceptionally that the record of a case is such as to afford intrinsic evidence that the mere statement that mental disorder did or did not occur justifies implicit confidence.

The pathological demonstration of mind-controlling centres must rest upon the evidence afforded by an examination of that smaller group of cases in which unmistakable mental derangement or decadence co-exists with well-defined structural lesion essentially confined to a limited cerebral area. This group, while small in comparison with the whole number of cases which, in the series analyzed, were found on post-mortem examination to have involved the frontal lesion, still comprises a very considerable number—a number much larger than that upon which the localization of a speech centre is founded. Further, the number of cases which have been found to be apparently exceptional to the law which it is sought to establish is both relatively and absolutely smaller than in case of that accepted for the speech centre.

No clinical observation has yet been recorded which suggests the specialization of control of any individual faculty of the mind, except that of articulate speech, in an individual convolution, and there is nothing to indicate a probability of any such localization in the future. These faculties are inseparably associated and interdependent, and in the absence of isolated action independent control would seem to be impossible.

The results of experiments which have been instituted by physiologists to determine the function of the frontal lobes have been contradictory or at least variously interpreted. The motor centres in the posterior frontal region, without doubt, have been well established; but no unanimity of opinion obtains among physiologists as to what centres, if any, reside in the prefrontal region.

The physiologists who have investigated this subject may be classified for the present purpose, without regard to other differences of opinion, as those who do, and those who do not, believe that their experiments upon the lower animals have shown mental decadence to have resulted from destruction of the prefrontal lobes. The first class includes Hitzig, Horsley, Schaffer, Ferrier, Bianchi, and Wundt; the second, Munk, Luciani, Meynert, Goltz, and Moolman.

Within these classes opinions widely differ. Ferrier does not admit that the mental deterioration indicates the existence of special centres of intelligence, and regards it as essentially a defect of the faculty of attention dependent upon frontal centres which control movements of the head and eyes. Bianchi attacks the views of Ferrier, and regards the prefrontal lobe as "the centre for the highest psychical functions." Munk and Luciani believe this lobe to be the controlling centre for the dorsal muscles. Goltz agrees with Ferrier in denying the specialization of centres of intelligence; and Hitzig, like Bianchi, affirms their existence. No two observers are exactly in accord. Such diverse interpretations of what must be essentially the same post-operative phenomena are explicable in great part by the difficulty experienced in estimating changes in the exercise of the imperfectly developed mental faculties of the lower animals; and in part, perhaps, in distinguishing from each other movements controlled by higher or lower centres. The weight of authority undoubtedly supports the contention that destruction of the prefrontal lobes is followed by mental decadence.

The mutual dependence and complementary value of pathological observation and of physiological experiment have been generally recognized. The precise delimitation by the physiologist of cerebral areas of control for muscular movement and for the special senses was first suggested by the observation of pathic conditions, and was verified later for the human subject by a recurrence to the methods of the pathologist. In the matter of localizing the control of the mental faculties, physiology has borne a comparatively unimportant part. The discovery of a speech centre, since animals do not talk, was necessarily independent of experiment. The limitations of this means of investigation for localizing the other mental faculties were indicated when referring to some of the causes of a divergence of physiological opinion. The results of physiological experiment, though not always recognized as the same or interpreted in the same way, may be regarded, however,

as corroborative of the fact substantiated by clinico-pathological observation, that mental decadence follows destruction of the prefrontal region. No experiments have been undertaken designed to show whether this deterioration would be equally manifest after the destruction or ablation of either frontal lobe while the integrity of the other was preserved. Such an experiment was incidentally made by Bianchi in one instance in which the lobes were successively removed; but, as has similarly happened when one lobe in the human subject has been destroyed by accident or disease, the obvious inference was disregarded. In one of four cases detailed by him, that of a young female cynocephalus,[1] the right frontal lobe was excised some months before the excision of the left. The primary operation was done August 2d, and the right lobe excised through a plane 2 or 3 millimetres in front of the excitable area for the arm, face, and jaws. One week later recovery had taken place, and her condition was in all respects normal, "save that she was subject to fear and had left external hæmianopsia."

September 11*th*. She was "still alert, agile, and observant," and no mental change occurred afterward except that she became more irritable.

January 31*st*. Six months later the left lobe was excised through a plane immediately in front of the face centre, as determined by electrical reactions.

February 2*d*. "When called she raises her hand slowly, opens her eyes, looks about, and relapses into the same condition. When touched she does not try to escape or look around."

9*th*. She is "duller and heavier. Intellect: Attitudes stupid, loss of physiognomical expression; apparently aimless walking; she ran incoherently from one end of the room to the other; pieces of plaster offered to her are taken and eaten as if they were sugar. In all her actions there seems to be a defect of perception, which seems to be reduced to a mere elementary level, and lacks some of the factors necessary to the formation of a more complete judgment. Her psychical life seems to be reduced to the existence of actual sensations."

May 4*th*. Animal killed by chloroform.

Bianchi has elsewhere declared: "No perceptible differences were noted in the behavior or psychical manifestations of animals mutilated on one side only."

It would be of interest to know if in any case it was the left side which was alone removed. If he found no psychical deterioration to follow left unilateral mutilation it would probably indicate that functional compensation was more immediate and more perfect in the right lobe than in the case of the human subject. It would be impossible to

[1] Brain, vol. xviii. p. 511.

admit that any negative experimental result could outweigh the positive evidence afforded by the study of human pathology. Conditions are morphologically and psychologically different. Muscular contraction is a physiological function, definitely circumscribed, common to man and to all animals, and known to be governed by the same recognized laws. The development of the mental faculties in the inferior animals, on the contrary, is very limited, and knowledge of the conditions which control their exercise is more limited still.

It is unnecessary for the present purpose to enter upon a discussion of theories which seem to have been disproved by pathological facts. The speculative views of Ferrier, however, which form a basis of belief for all those who deny the existence of special centres of control for the mental faculties carry too great a weight of authority to be ignored. It may be recalled, in brief, that he regarded the sensory and motor centres of the whole cerebrum as the "substrata of sensory perception and ideation, and of acts of volition as well as feelings associated with their activity." He concluded, as the result of experiment, that the prefrontal lobe is the motor centre of the eyes and head on the opposite side, and, in consequence of the close relation between the movements of these parts and attention, that it is also the centre for that faculty. He declared that it would be "absurd to speak of a special seat of intellect or intelligence in the brain;" and that "the control of ideation and the power of attention form the basis of all those intellectual achievements not included in mere receptiveness, ideational or emotional mobility, and the facility of executing delicate and complex motor acts."[1]

It is to be objected to the theory of Ferrier not only that it is not founded on pathological observation, but that it affords no explanation of the origin or control of abstract conceptions, moral sentiments, or congenital peculiarities of character. It may be difficult to disassociate mental operations from external impressions; but certainly obstinacy, selfishness, and generosity, or other qualities which are innate, and reasoning processes which involve purely spiritual conceptions, cannot be evolved from the perception of external objects or associated with muscular movements. In like manner, comparison, judgment, or the appreciation of moral qualities is as far from a mere conscious sensation as it is from an automatic movement.

Ferrier's views have been modified by some writers, and by others have been rejected altogether. Bianchi[2] not only holds that "the prefrontal lobe is the centre for the highest psychical functions," but that "there exists no centre the function of which is to inhibit, and that there exists no faculty of attention." Boris Sidis,[3] in a discussion of

[1] Functions of the Brain, 1886, pp. 460-467.
[2] Brain, vol. xviii. p. 497.
[3] Psychology of Suggestion, New York, 1899, pp. 124-128.

hypnotic amnesia, rejects entirely the theory of retention and reproduction of images by modifications of nerve elements as the essentials of memory.

Ferrier expressed the opinion that it was not necessary to assume higher centres in this region in order to explain the facts either of normal or abnormal mentation. In the progress of events clinical observers have learned that this necessity exists; and the present review of a multitude of clinical cases shows, further, that it is necessary to assume their localization in the left prefrontal lobe, to the exclusion of the right.

"One clear case," to quote again from Ferrier,[1] "in which destruction of a region had caused no cessation or disorder of a function would be sufficient to overcome our conclusion," which in this case is, as above stated, that the exclusive control of mind is resident in the left prefrontal lobe. Not only has no such clear case been found, but none in which limited lesion of the right prefrontal lobe or any other cerebral area has produced symptoms of mental disorder.

It is immaterial, so far as it concerns a control of the mental faculties in the prefrontal region, whether the function of the left prefrontal lobe is one of co-ordination or one of inhibition, or whether it is a direct control of mental, moral, and emotional phenomena comparable to the control of motility in the motor areas, as asserted by Bianchi, or whether it is a control of sensorimotor processes, which are the anatomical substrata of mentation, as insisted by Hughlings Jackson. It is simply a question of topography, entirely independent of psychological considerations. It has no concern either with Tyndall's "unthinkable passage from the physics of the brain to the corresponding facts of consciousness," with Lewes' assertion that "the neural process and the feeling are one and the same process viewed under different aspects," or with Jackson's[2] parallelism of mental and subjacent physical states. The fact that mentation has an anatomical substratum having been universally accepted as an almost axiomatic truth, there remained for the determination of the neural physiologist and the pathologist the more or less precise delimitation or the general diffusion in the cerebrum of this physical basis.

Three propositions are justified by the cases which have been presented:

1. The more absolutely the lesion is limited to the left prefrontal lobe the more positive and distinctive are the symptoms of mental default.

2. The integrity of the mental faculties remains unimpaired in right

[1] Localization of Cerebral Disease, 1878, p. 3.

[2] See Hughlings Jackson on the "Localization of Movements in the Brain." London. Reprint from The Lancet, 1873.

frontal lesion, though it involves the destruction of the entire lobe, or even extends to the entire hemisphere.

3. The exceptional instances in which seemingly opposite conditions exist are always reconcilable, on more careful examination, with the assertion of an exclusive control of the mental faculties residing in the prefrontal region of the left side.

If, then, the same nature and degree of proof which is deemed sufficient for the localization of other cerebral functions may be accepted in case of the mental faculties, their centre of control has been established.

THE UNILATERAL OCCURRENCE OF KERNIG'S SIGN AS A SYMPTOM OF FOCAL BRAIN DISEASE.

By Joseph Sailer, M.D.,
MEDICAL REGISTRAR TO THE PHILADELPHIA HOSPITAL.

I desire to report two cases in which Kernig's sign was present only on one side and appeared to bear some reference to a cerebral lesion on the other side of the brain. This sign was described by Kernig in 1883 before the Medical Society of St. Petersburg, and the next year published in German. His attention was first directed to the phenomenon in a patient recovering from epidemic cerebro-spinal meningitis. This patient could walk perfectly well, could lie in bed with legs extended, but whenever she sat in a chair she found it impossible to extend the legs on the thigh beyond a right angle. Subsequently he studied fifteen cases of meningitis, nine of which were confirmed by autopsy, with reference to this sign, and found it present in all. It could be elicited whether the patient sat up, lay on the back or on the side. He describes it as a flexion contracture in the legs (and occasionally in the arms) when the thigh is flexed to a right angle upon the trunk. Under these circumstances any attempt to extend the leg on the thigh meets with severe resistance as a result of contraction of the hamstring muscles, and it is impossible to extend the leg beyond an angle of 135°, or even, in extreme cases, beyond a right angle. When the thigh is extended the hamstring tendons are relaxed and soft; when, however, the thigh is at a right angle to the trunk and an attempt is made to extend the leg they become tense and prominent. The contraction is not ordinarily associated with pain, nor with any increased rigidity in any other part of the body, and Kernig particularly noted that the retraction of the head did not become greater when the patient sat up. He states that the sign usually persists long into convalescence; it may vary from time to time in the course of the disease; it is not produced by mechanical irritation of the sciatic nerves, and may, as he noted in his original

communication, occur in certain other conditions, although in all of those that he observed there was reason to believe that irritation of the membranes existed.

The literature on the subject is very inconsiderable, although the presence or absence of the sign is now usually mentioned in connection with a suspected case of meningitis. The first important article on this subject was that of Friis, who found it present in 74 of 86 cases, and was not able to exclude it positively in all of the other 12. Henoch also obtained it frequently in children suffering from meningitis, and Blumm mentions its existence in 7 of 9 cases. In one case the contraction of the muscle came on suddenly and was painful. Bull obtained it in all positions in 2 cases: one a tumor of the cerebellum and the other a thrombosis of the left lateral sinus. Netter, in an extensive series of investigations which practically called general attention to the existence of the sign, found it present in nearly all cases of meningitis. The attention of the American profession was directed to this subject by a paper by Herrick, read before the American Medical Association. He found it present in 17 of 19 cases of meningitis and only twice in 100 other cases, one of which was a case of subdural hemorrhage, and one a case of gonorrhœal rheumatism, as a result of which the patient had lain with the knees flexed for a period of four weeks. He failed to observe it in cerebral hemorrhage, brain tumor, and other intracranial conditions. In other cases the absence of the sign was of great value in excluding meningitis. He called renewed attention to the fact that the sign can be elicited if the patient either sits or lies down. Its presence has also been reported by Widal and Merklen in a case in which the lesion was found to be a clot pressing upon the anterior surface of the pons and medulla, and by Thyne in a case in which there was hemorrhage into the left lateral lobe of the cerebellum, and an effusion of blood over the right occipital lobe and into the fourth ventricle. The patient also had retraction of the head, but meningitis was not present. The sign is more often absent in tuberculous than in any other form of meningitis. Henoch was the first to mention this fact. Netter, Herrick, and Dieulafoy have all confirmed it, and Packard has reported 3 cases of tuberculous meningitis in children aged fifteen, sixteen, and four months, in which the sign was persistently absent. With the exception of one of Herrick's cases, in which the sign was elicited in the unaffected leg of a woman suffering with gonorrhœal gonitis, mention has not been made of its unilateral occurrence.

During the past year I have had under my care in the wards of the Philadelphia Hospital, two cases in which the sign was unilateral and appeared to be a symptom of focal encephalitis. The cases are intrinsically interesting, but possess no common points except this peculiar phenomenon.

CASE I.—The patient, W. H. P., a white man, aged twenty years, laborer by occupation, was admitted to the Philadelphia Hospital on September 16, 1901. He was partially delirious, but could answer simple questions. He complained of severe headache and pains all over the body. The temperature on admission was 104°; there was slight abdominal tenderness and an occasional dry cough. His family history was indefinite; his mother had died of Bright's disease; one sister was dead; his remaining relatives were living and well. His previous history was obtained from his father, who stated that he had had whooping-cough, chicken-pox, measles, and malaria in childhood.

In 1888 he had a moderately severe attack of typhoid fever, and at Christmas, 1899, an attack of what was diagnosed as spotted fever, which lasted for about three weeks. This came on suddenly, and it was necessary to bring him home in a patrol wagon. There was a doubtful history of an attack of appendicitis about a year ago, for which no operation was performed. For four or five weeks before his present illness he had been working on an ice-wagon. The history of his present condition was as follows: For about two weeks he had been complaining of pain in the side, backache, and headache. On September 14th he came home from work complaining of intense headache, and soon became delirious; he was not able to sleep, and on the 15th became violent. He had a serous diarrhœa, with watery, yellowish stools, and seemed to be very feverish. Upon admission the following notes were made: A well-developed, well-nourished male; numerous tattoo marks on both arms; pupils equal, react to light and accommodation; tongue heavily coated, protruded in a straight line without tremor. Pulse was strong, regular, of good volume and good strength; chest was well formed, expanded equally and well. The abdomen was negative, with the exception of slight tenderness in the right iliac region. No nervous symptoms were noted on this day. On the following day, however, when I first saw the patient, he was acutely delirious. The head was slightly retracted, although the muscles of the neck were not hard. The pulse was of medium volume. The left arm was strongly flexed and distinctly rigid. The right arm was normal. The lungs were normal; the cardiac dulness commenced at the third interspace and extended laterally from the mid-sternum to the left parasternal line; there was a weak, diffuse apex-beat in the fourth interspace. Auscultation revealed gallop-rhythm, and a slightly accentuated pulmonic second sound. The liver extended from the sixth rib by the costal border; the spleen was not palpable, but was slightly enlarged to percussion. The stomach, examined by auscultatory percussion, did not extend below the costal border; there was no eruption on the skin; the inguinal and post-cervical glands were small but palpable. There was slight hyperæsthesia over the abdomen. The supra-orbital nerves and the suprabulbar fossæ were not tender, and the patient did not manifest any discomfort upon strong percussion of the skull. The reflexes were not exaggerated. Kernig's sign was readily elicited in the left leg. It was possible to extend the right leg in an almost straight line with the thigh when the latter was flexed at right angles upon the abdomen. Posteriorly nothing abnormal was noted aside from a slight increase in vocal resonance at the base of the left lung, and numerous subcrepitant râles at both bases. A provisional diagnosis was made of tubercular meningitis, associated with hypostatic conges-

tion of the base of the left lung, and with acute nephritis. On September 18th the patient was distinctly worse; he had been delirious all night, and slept only for short intervals; he complained of pain in the precordial region; there were still signs of hypostatic congestion of the lower lobe of the left lung posteriorly. When roused there was distinct lagging of the left upper eyelid. The mouth was drawn toward the right side, and the right side of the face was wrinkled, while the left side was smooth. The reflexes were not changed. The following day the head was turned to the left side; the left pupil was smaller than the right and seemed sluggish. The tongue was dry and rough and protruded to the left side. There was marked flexor spasm in the left arm, which also seemed to be paretic, at any rate the patient did not use it to remove irritants. The right arm was moved freely and appeared to be normal. The knee-jerks were slightly increased, especially on the left side, and Kernig's sign was distinctly present in the left leg, which in addition was slightly paretic. The patient now had incontinence of urine. On September 20th the condition was about the same; the head was turned strongly to the left and could not be forcibly turned in the other direction. The left arm was firmly flexed at the elbow, and resisted straightening. The right leg was not moved voluntarily; in the left leg occasional irregular movements were noted. Kernig's and Babinski's signs were both present on the left side but not on the right. The apex-beat was in the fourth interspace, in the nipple line. A systolic murmur was heard on this day for the first time, most distinctly at the apex, and there was moderate accentuation of the second pulmonic sound at the base. At midnight of this day the patient had a hemorrhagic eruption over the entire body, consisting of very slightly raised, small round spots that did not disappear upon pressure. There were also hemorrhages under the conjunctivæ, and in the mucous membranes of the lips and mouth. The patient could not be roused, and it is possible that he was deaf on both sides. The head was retracted and rotated to the left; the right pupil was widely dilated and reacted promptly to light; the left was contracted and reacted very slowly; there was chronic drooping of the left eyelid. Respiration was of the typical Cheyne-Stokes variety. The pulse showed a very remarkable alteration, it was full, rapid, and receded quickly—a typical water-hammer pulse. Upon auscultation of the heart a loud systolic murmur could be heard at the apex and at the pulmonic cartilage; there was also accentuation of the second pulmonic sound. The left arm was flexed over the chest and could not be extended by force; the right foot was not moved even when the sole was vigorously irritated. There was marked ankle clonus on both sides. The knee-jerks were increased, more on the left side. Kernig's sign and the Babinski phenomenon were both present only on the left side. The patient was entirely unconscious and only groaned occasionally. On September 21st he grew gradually weaker, the pulse becoming smaller; respirations, however, were slightly more regular; the reflexes remained increased until death, which occurred at 6.40 A.M.

During the course of the case the urine was examined on the 17th and found to contain albumin and numerous granular and blood casts. The specific gravity was 10.14. On the 17th the leucocytes were 17,600; on the 19th, 27,000. The Diazo reaction was tested on the 18th and was not present. Blood was taken for the Widal reaction

on the 18th, and the report returned from the City Laboratory on the 20th that it was not present. On the 20th, Dr. Pfahler made a spinal puncture and also withdrew some blood from the median basilic vein of the right arm, under strict aseptic precautions. Agar tubes were inoculated with this material, and on all of them cultures of a staphylococcus that became golden-yellow appeared. These cultures were pure. On the 21st the autopsy was made by Professor Coplin, who has kindly permitted me to abstract his notes. Rigor mortis was unusually pronounced; the pupils unequally dilated, the left more than the right. The whole body was covered by a petechial eruption which involved all the visible mucous membranes. Upon opening the body hemorrhages were found in all the serous membranes. The right side of the heart was slightly dilated; the tricuspid, pulmonic, and mitral valves were normal. The anterior and left aortic leaflets were partially destroyed, and the edges showed recent inflammatory vegetations. Upon the remaining leaflet only the ventricular surface was involved, and it was slightly rough and contained a few small vegetations. The left lung contained an infarct upon the lower edge of the upper lobe; the lower lobe showed intense hypostatic congestion. The spleen was enlarged and soft; the kidneys showed cloudy swelling; the meninges were congested, and there was a softened area in the motor region on the right side. The right tibia was slightly deformed, and upon incision was found to be the seat of an old osteomyelitis, the marrow having been largely converted into compact bone, and the compact substance being unusually dense.

The autopsy, therefore, confirmed the final diagnosis as far as the heart, kidneys, and lung were concerned. We had supposed during life that a meningitis existed, and as a matter of fact the membranes were intensely congested and œdematous, and over a small area of the ascending frontal gyrus at the level of the second frontal convolution they were slightly altered. The main lesion in the brain, as subsequent examination showed, consisted of an area of hemorrhagic softening in the middle of the ascending parietal convolution, and extending inward through the centrum ovale toward the internal capsule, which, however, it did not involve. Surrounding this there was an area a few millimetres wide, of partial discoloration of the brain, apparently due to œdema. At the autopsy Dr. Coplin permitted me to make cultures from the brain and gall-bladder, and from both an organism was obtained which was similar in all respects to the one obtained by Dr. Pfahler in his cultures from the blood and cerebro-spinal fluid. This organism has twice been injected into rabbits, once intravenously, without producing fatal effects. Dr. Coplin also made cultures from the heart blood and spleen, and obtained a coccus culturally and morphologically identical with the staphylococcus pyogenes aureus. Sections through the brain showed that the lesion consisted of an area containing considerable hemorrhagic extravasation that was surrounded by a layer of polynuclear cells, in the midst of which there were numerous masses of cocci. The surrounding brain tissue showed swelling of the ganglion cells and thickening of the glia. The case, therefore, is a rather interesting example of acute malignant endocarditis, due to staphylococcus infection, and associated with a focal encephalitis. In view of the existence of a chronic osteomyelitis of the right tibia it is perhaps permissible to suspect, in the absence of

any other focal lesion, that possibly the organism remained latent in this situation, and then, for some reason, invaded the body, producing the endocarditis and subsequently the various pyæmic manifestations. Unfortunately cultures were not made from the bone lesion.

CASE II.—J. P., white, aged thirty-seven years, was admitted to the hospital on November 16, 1901, complaining of pain in the back and partial loss of power in the left side of the body. The patient is an intelligent man who had been healthy until a year ago, when he occasionally had attacks which were diagnosed as rheumatism, and a fistula in ano. He has used alcohol to excess; he denies venereal history, and is the father of four healthy children. Three weeks before admission to the hospital the patient, who at that time was in good health, went to bed with a feeling of general malaise and pain in the back and limbs. On the following morning he discovered that he was unable to use the left side of the body; speech was thick; he still had pain in the back and also in the left arm and leg. Physical examination on December 7th showed slight inequality of the pupils, the right being the larger, although both reacted to light and accommodation. The tongue was protruded in a straight line; the supra-orbital reflex was equal on both sides; there seemed to be slight impairment of motion on the left side of the mouth. Speech was defective, the utterance was thick, and there appeared to be special difficulty in pronouncing the letter "R." This, the patient says, has developed since his present sickness. The platysma moved freely on both sides and there was slight rigidity of the muscles of the neck on the left side posteriorly. There was permanent spasticity of the muscles of the right arm, and of all the muscles controlling the left wrist-joint; although the flexors were more involved, and the arm was therefore held completely flexed with the wrist bent at right angles. There was no rigidity of the fingers of the left hand, excepting some spasticity of the long extensors of the thumb. The muscles appeared to be slightly wasted; the grip was weak; the movements of the arm were weak, and the patient was unable to extend it beyond a right angle, although it could readily be extended by the application of force. The biceps jerk was diminished; the triceps jerk was slightly exaggerated, but the muscles did not show mechanical irritability. There were no sensory disturbances in the arm, and all the muscles of the arm and shoulder responded readily to faradic electricity. Aside from the hampering effect of the spasticity, motion was normal, and there was no evidence of inco-ordination. The stereognostic sense was normal. Whenever an effort was made to move the left arm the patient moved the right arm with it in a somewhat similar manner, and this associated movement could not be controlled voluntarily. The right arm was entirely flaccid; movements were normal and were not accompanied by movements of the left hand. The little and ring fingers were persistently flexed on the palm, and there was wasting of the thenar and hyperthenar and interosseii muscles. This was evidently due to an injury to the ulnar and median nerves received fifteen years ago, the scar of which was still distinct. The thumb, index and middle fingers were capable of free movement, and the grip was fairly strong. There was slight numbness of sensation of the ulnar side of the hand. The arm reflexes were normal; sensation was entirely normal. The left leg was distinctly spastic; it was held habitually in a position of extreme extension. The knee-jerk was greatly exaggerated; there

was persistent patellar clonus, and a rapidly exhausted ankle clonus. Babinski's phenomenon was present to an extreme degree; the plantar reflex was normal. The movements of the leg were executed slowly and clumsily, but without any evidence of inco-ordination. The toes did not resist passive movement in any direction. Sensation was everywhere normal; localization was good, and the muscle sense was not destroyed. When the thigh was flexed upon the abdomen the leg could not be extended beyond an angle of 90°; if the patient sat on the edge of the bed it was impossible to extend the left leg beyond a perpendicular position. Whenever this sign was tested the hamstring muscles, which were soft and relaxed when the leg was extended, became hard and rigid. The spasm was not associated with any pain. Kernig's sign had been tried daily since it was first elicited, and the angle through which the leg could be moved diminished from an estimated 115° on November 22d, to between 90° and 95° on December 6th. The right leg was flaccid; the knee-jerk was exaggerated; patellar clonus could not be elicited, and there was no ankle clonus. The Babinski reflex was distinct and characteristic; there was no impairment of co-ordination and no disturbance of sensation. The muscles of both legs responded readily to faradic electricity. The muscles of the ulnar side of the right hand failed to respond. The abdominal reflex was present and apparently normal. The patient states that his memory is not as good as it formerly was; he has occasional emotional attacks apparently due to a realization of the serious nature of his disease, but is otherwise cheerful and exceptionally intelligent. He has complained of diplopia ever since his admission, and an examination by Dr. de Schweinitz on December 4th showed that the vision in each eye was reduced to 5/15, and there was a paresis of 8 prism degrees of the left external rectus. The eye-grounds were normal, and there were no changes in the form fields.

On December 20th, the condition of the patient had improved considerably. The diplopia was rarely present excepting at night; the rigidity of the left arm persisted; both knee-jerks were moderately exaggerated, and there was slight spasticity of the left leg. Kernig's sign had completely disappeared, and in spite of the spasticity it was possible to extend the left leg completely. The patient was able to walk with assistance; speech showed distinct improvement, but he was still very emotional.

The nature of this case is somewhat obscure. The lesion is evidently located in the upper portion of the medulla on the right side, and extends far enough forward to involve the nucleus of the left abducens. It cannot be complete because the paralysis is not complete on the left side, and it must be limited because there is no disturbance of sensation. Tumor was at first suspected, and the patient stated that at the commencement of his attack he had headache and vomiting; this, however, soon disappeared, and the absence of choked disks rendered the diagnosis of tumor unlikely. There is no reason to suspect embolism of one of the branches of the basilar artery, but thrombosis of this artery or syphilitic disease of the artery causing partial degeneration in the surrounding tissue cannot be excluded. The sudden onset of the attack leads me to suspect the possibility of a non-suppurative focal encephalitis of the type described particularly by Nonne.

The patient has received potassium iodide in increasing doses since admission. There is, however, no other reason to suspect a syphilitic

lesion, for the patient has no recognizable signs of syphilis. The most interesting feature is the presence of Kernig's sign while the symptoms were severe, and its disappearance as improvement progressed.

The nature of the mechanism by which Kernig's sign is produced is still obscure. Kernig himself did not attempt any explanation, but was content to prove that it was not due merely to increased intracerebral pressure, nor to pressure upon the sciatic nerves. Friis suggested that it was due to irritation of the corda equina by the infected cerebro-spinal fluid. Of course, the occurrence of the sign in purely cerebral lesions renders this view untenable. Henoch spoke of it as a reflex manifestation. I do not know exactly what he means by this, but there can be no doubt that the position of the thigh which stretches the flexor muscles evidently produces at a certain point a contraction in them. To call this a reflex does not explain the sign. Exactly the same view has been maintained by Bull, who called attention to the fact that it is difficult fully to extend the leg when the thigh is at right angles to the trunk, and regards the sign merely as an exaggeration of this normal condition. Netter and Herrick, who next to Kernig and Friis have made the most extensive investigations upon this subject, merely discuss the theories that have been suggested by others. Widal and Merklen look upon it as a manifestation of irritation of the spinal meninges, but do not attempt to explain how this irritation produces the very peculiar phenomenon. Chauffard, the most recent author to discuss its nature, explains it as an exaggeration of normal phenomena, due to a hypertonicity of the muscles. It is closely analogous—according to him—to the retraction of the muscles of the neck and back, and he therefore defines it as a contraction mono-regional or multi-regional affecting physiologically predominant groups of muscles, and occurring in attitudes which normally bring these muscles into play.

In the case that I report the common feature was the spastic paresis of one side of the body due to unilateral cerebral lesion. In both cases this spasticity did not produce any retraction of the hamstring muscles when the leg was extended, but gave rise to all the characteristic phenomena of Kernig's sign when the thigh was flexed upon the trunk. In the majority of other cases in which this sign occurred there is reason to suppose a certain degree of irritation of the pyramidal tract associated with depression of its conductile power, that is to say, a condition similar to the one that existed in both of these cases, a spastic paresis. And it seems not unreasonable to suppose that more extensive and careful observations will show that in the majority of cases Kernig's sign may be regarded as one of the symptoms of a partial lesion of the pyramidal tract, that is to say, a lesion which does not destroy it but which prevents its complete functional activity. This does not serve to explain its mechanism, unless we assume with Bull and Henoch that

it is merely an exaggeration of normal conditions; but to assert this positively is of course at present unwarranted. Its mechanism is still as uncertain as is the mechanism of Babinski's sign, which in some respects is analogous to it, but apparently is present when the lesion of the pyramidal tract is much more severe than is compatible with the existence of Kernig's sign. Kernig is the only author who states that the arms may be affected by similar condition. In the two cases which I report there was a flexor spasm in the arms on the affected side, but in both cases this could be overcome by force, was persistent, and bore no definite resemblance to the manifestations in the leg.

It is of course obvious that it is not a lesion of the meninges but of the subjacent nervous substance that causes the occurrence of Kernig's sign. Practically all cases of leptomeningitis are associated with a more or less severe degree of encephalitis. As far as I know, however, the occurrence of the sign in the course of a typical case of encephalitis has not been recorded. In Nonne's series of cases no mention whatever is made of it, although he distinctly states that in one or two cases symptoms of meningitis were not present. Whether this includes the sign or not is of course impossible to determine. It is impossible to say whether the sign is frequently present in encephalitic lesions involving the pyramidal tract or not; that it may occur in such cases, Case I. sufficiently proves, and Case II. supports the affirmative view, although, of course, the diagnosis has not been confirmed by autopsy. At any rate, I think the following conclusions are justified: First, Kernig's sign may occur as a symptom of focal encephalitis, and in this condition may be present upon only the opposite side of the body. Sometimes it is associated with spastic paresis of the leg upon that side. Second, in these cases there may be a persistent tonic spasm of the flexor muscles of the arm, which, however, does not resemble Kernig's sign in its mechanism. Third, the most reasonable explanation of Kernig's sign that we have at present is to ascribe it to an irritative lesion of the pyramidal tract that diminishes but does not destroy its functional activity.

At my request, my resident physician, Dr. Shields, has made careful studies of 100 cases at the Philadelphia Hospital, with reference to the presence of Kernig's sign. The results of these studies are appended to this article.

In addition, Dr. Clark has, at my request, reported three cases of meningitis, all confirmed by autopsy, in which the sign was absent during the entire period of observation.

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REPORT OF ONE HUNDRED CASES, ALL NON-MENINGITIC, EXAMINED FOR KERNIG'S SIGN.

BY WILLIAM G. SHIELDS, JR., M.D.,
RESIDENT PHYSICIAN TO THE PHILADELPHIA HOSPITAL.

THIS report is to show the result of the examination of 100 non-meningitic cases, both febrile and afebrile, for the presence of Kernig's sign. In every case both legs were examined for the sign in both erect and recumbent postures, excepting when the condition of the patient would not admit his sitting up. In 5 cases Kernig's sign was present; 3 showed the sign unilaterally, and 2 bilaterally, 1 case of uræmia and 1 case of typhoid fever, and it is interesting to note that in both of these cases the sign could not be obtained after recovery. Kernig's sign persisted in the 3 remaining cases—2 cases of right-sided hemiplegia, and 1 of typhoid fever—and in all it was obtained on only one side. The case of typhoid fever is still quite ill, and it is possible that the sign will have disappeared by the time the patient has regained her normal condition. In both cases of typhoid fever which showed the sign, delirium was marked and persistent. This predominance of mental symptoms may have been an indication of febrile or toxic cerebral irritability, which might have in some manner been accountable for the presence of the sign.

Number of cases of each.		Diagnosis.	Right leg.	Left leg.	Angle of extension.
1		Cirrhosis of liver	—	—	—
(Case No. 4) 1		Hemiplegia (right)	+	—	115°
(Case No. 5) 1		Hemiplegia (right)	+	—	120
3		Influenza	—	—	—
2		Malaria	—	—	—
8		Pneumonia	—	—	—
4		Rheumatism	—	—	—
48		Senile	—	—	—
25		Tuberculosis	—	—	—
(Case No. 1) 1		Typhoid (B. E. P.)	—	+	105
(Case No. 2) 1		Typhoid (J. W.)	+	+	110
3		Typhoid	—	—	—
(Case No. 3) 1		Uræmia (J. C.)	+	+	110
1		Uræmia	—	—	—
100					

The table shows the diagnoses of the cases and the number of each examined. The condition in each leg with regard to the presence or absence of Kernig's sign is noted, and in those cases in which the angle of extension was 120° or less this fact has been stated. Brief reports of the 5 positive cases are given.

CASE I.—C. E. P., girl, aged thirteen years, was admitted to the hospital with a history of having been ill for about five weeks. She suffered from malaise, headache, pain in the chest, abdomen and legs, and for about a week she had had epistaxis, and nausea and vomiting for about three days. There were constipation, cough, and expectoration of a mucopurulent material. Two other persons were ill with typhoid fever in the same house. The patient was pale, the pupils were large and reacted to light and distance. The tongue was dry and coated; there was marked hyperæsthesia on the cutaneous surface, especially the arms and legs; high temperature, and a roseolar eruption on the chest and abdomen. The spleen was enlarged; Kernig's sign was present on the left side, the angle of extension not exceeding 105°. The leucocyte count was 5600. The Widal reaction was positive. On the third day after admission a loud systolic murmur was heard at the apex, and the pulmonic second sound was accentuated. Two weeks later she developed otitis media, and about the same time suppuration of the axillary glands. The patient gradually improved, and at present is convalescent, but Kernig's sign still persists in the left leg, the greatest angle of extension being 105°. The spasm is not painful.

CASE II.—J. W., white man, aged thirty-six years, an iron-worker by occupation. Patient when first seen was treated for alcoholism. After his acute alcoholic symptoms with consequent gastritis had subsided, he continued to have elevated temperature. His blood was examined for the Widal reaction and a positive report returned. He had only three typical typhoid spots distributed over the abdomen. He had constant pain in the head and limbs. Constipation was present all through the attack. No enlargement of the spleen could be determined. The tongue was thickly coated with a yellowish-brown fur. Delirium was present in a marked degree for a considerable time. The subsequent course of symptoms, signs, and temperature proved it to be an undoubted case of typhoid fever. The patient showed Kernig's sign typically on both the right and left sides during the height of the disease while lying in bed. Later in the course of the disease, when the patient's condition warranted his being placed in the erect posture, the sign was obtained when he sat on the edge of the bed. When lying in bed the greatest angle of extension was 105° on each side, whereas, when he sat up ten days later the legs could be extended to an angle of 115° with the thigh. This man recovered completely from his enteric attack, and at the end of convalescence Kernig's sign was not present on either side.

CASE III.—J. C., aged sixty-one years, a bricklayer. On November 3, 1901, the patient was admitted suffering from uræmia. He was unconscious, he could not be aroused, the pulse was rather small and fairly rapid. The eyes were rotated upward and to the left, the pupils being somewhat contracted. No reaction to light could be ascertained. The skin was dry and hot. The body temperature was somewhat elevated;

the tongue was dry, brown, and hard; the urine, obtained by catheter (6 drachms), showed a large amount of albumin, with numerous hyaline and granular casts. He was treated with ordinary uræmic therapeutics and rapidly regained consciousness. In two weeks' time he had improved so much that he required no special treatment or attention. When first examined he showed Kernig's sign on the right and left sides, the greatest angle of extension being about 110°. On the eighth day of observation this sign could not be elicited on either side. This patient was only examined for the sign when he was lying in bed, the thigh being flexed upon the abdomen at an angle of 90°.

Cases IV. and V.—The two hemiplegics referred to were both cases in which the mentality was below par. They were both rather typical cases of right-sided paralysis, which condition had lasted in one case for over twenty years, and in the other for about fifteen years. The mode of onset as well as the subsequent course of the affection could not be ascertained. They were examined, both when sitting up and in a recumbent posture, and Kernig's sign was found present on the right side in each case. In one case the greatest angle of extension was 115°, and in the other 120°. In both cases when the thigh was not flexed the leg could be extended to an angle of 180°.

In concluding this report of 100 cases it is essential to state that in no positive case was there any joint involvement either osseous or tendinous; also that in all these cases the legs could be fully extended, and when the thigh was flexed the tendons became hard and tense. I have called no case positive in which the angle was more than 120°. The only case on this list in which the presence of Kernig's sign might have proved misleading by resembling meningitis was Case I., in which there were delirium, elevated temperature, rapid pulse, a red eruption over the chest and abdomen, with hyperæsthesia of the arms and legs. A leucocytic count of 5600, with positive Widal reaction, and two persons ill with typhoid fever in her home at the same time, made the diagnosis clear.

THREE CASES OF MENINGITIS IN WHICH KERNIG'S SIGN WAS PERSISTENTLY ABSENT.

By F. S. Clark, M.D.,
RESIDENT PHYSICIAN, PHILADELPHIA HOSPITAL.

(From the service of Drs. Hughes and Salinger, of the Philadelphia Hospital.)

Case I.—D. C., Italian laborer, aged twenty-two years, had a severe chill associated with pain in the abdomen and headache. In a short time he became unconscious, and when admitted to the hospital one day after the onset, his eyes were open and staring, the pupils were dilated, the right slightly larger than the left. Both reacted to light and accommodation. There was some rigidity of the muscles of the neck which increased to marked retraction of the head as his symptoms progressed. Photophobia and hyperæsthesia were prominent

symptoms. There were herpes labialis, and sordes on the teeth, but no eruption on the skin. The knee-jerks were normal; Kernig's sign could not be elicited in either leg in the recumbent or erect postures. Lumbar puncture was performed on two occasions, and a turbid fluid containing pus cells withdrawn. Microscopical examination of this fluid for bacteria was negative. There was a leucocytosis of 15,000, and a slight albuminuria with a few hyaline casts. The patient died on the fifth day without regaining consciousness. At the autopsy there was venous congestion of the meninges, and there was an exudate upon the under surface of the cerebellum and on the thoracic portion of the cord. The dura mater was adherent to the skull.

Case II.—A. H., a salesman, aged twenty-three years, was suddenly attacked with vertigo associated with faintness and nausea. This lasted about five minutes. Similar attacks recurred at intervals, and he also complained of nose-bleed. Three weeks later when he was admitted to the hospital it was noted that his vision was impaired. He complained of dizziness; the gait was staggering and hesitating; the eye-grounds were reported to be characteristic of inherited syphilis, showing extensive exudative disseminated retinochoroiditis. Potassium iodide, however, produced no effect. Speech was hesitating; there was occasional vomiting; the knee-jerks were increased, and patellar clonus was present on the right side, and ankle clonus on both sides. Babinski's sign and Kernig's sign were not present. There was no retraction of the head, no loss of consciousness, but speech became more and more impaired, and the patient died in the fourth week of the disease. The autopsy showed the presence of a subacute tuberculous leptomeningitis. The membranes at the base of the brain were very adherent, and were separated with considerable difficulty. A few old calcified tubercles were found in the lung, and the right lobe of the liver showed some old healed tubercles.

Case III.—T. B., an Englishman, aged forty-eight years, a tailor by occupation. Two days before admission he had become violent and had destroyed the furniture of the house. On admission he was unconscious, delirious, and there was continual twitching of the hands and feet. The thoracic and abdominal organs were normal. Four days after the onset of the disease he developed marked retraction of the head, but the reflexes were normal. Babinski's sign was not present and Kernig's could not be elicited. Lumbar puncture was performed on two occasions, and the tubercle bacillus was found in the clear fluid withdrawn. There was slight albuminuria and a few casts. The patient died on the seventh day, and at the autopsy miliary tubercles were found in the pia mater, and tuberculosis of the left lung, the liver, the spleen, and the kidneys.

Briefly summarized, there is one case of acute cerebro-spinal leptomeningitis whose bacterial nature was not determined, and two cases of tuberculous meningitis. In all of these cases Kernig's sign was repeatedly tested and was never present, no difficulty being experienced in any instance in extending the leg beyond an angle of 150°. This extension did not cause undue prominence of the hamstring tendons, nor apparently hurt the patient. The cases confirm the opinion that Kernig's sign is especially unreliable in tuberculous meningitis.

THE TREATMENT OF THROMBOSIS OF THE LATERAL SINUS FOLLOWING MIDDLE EAR SUPPURATION.[1]

By Edward Bradford Dench, M.D.,
PROFESSOR OF OTOLOGY, UNIVERSITY AND BELLEVUE HOSPITAL MEDICAL COLLEGE; AURAL SURGEON TO THE NEW YORK EYE AND EAR INFIRMARY; CONSULTING OTOLOGIST TO ST. LUKE'S HOSPITAL AND TO THE NEW YORK ORTHOPEDIC DISPENSARY AND HOSPITAL.

Up to about ten years ago the infection of intracranial venous channels following an inflammatory process within the middle ear and mastoid was looked upon as an almost necessarily fatal complication. At this time operative otology was in its infancy. The aural surgeon was exceedingly loath to institute any radical method of treatment for the relief of middle-ear suppuration. Even incision of the drum membrane for the evacuation of pus within the tympanum was looked upon as a somewhat grave procedure, and was resorted to only in cases where, after a long period, nature did not evacuate the abscess by means of spontaneous rupture of the membrana tympani. When it became evident that the inflammatory process had extended into the osseous structures adjacent to the ear—that is, into the mastoid cells—the surgeon was even more loath to employ radical measures to relieve the disease. An operation having for its purpose the thorough cleaning out of the mastoid cells and the securing of free drainage of the tympanum through a posterior opening was only resorted to at the very last moment, and was then looked upon as a grave procedure.

Schwartze[2] may be looked upon as the pioneer in mastoid work; he was the first to lay down the indications for operative interference upon the mastoid and to formulate a rational operative technique. While the indications for the necessity of operative interference have undergone no essential modifications during the last decade, the technique of operation has naturally been greatly improved.

The original Schwartze operation consisted in thoroughly opening the mastoid antrum and establishing through-and-through drainage, in most cases, between the posterior opening and the external auditory meatus, although this was not insisted upon absolutely. As time went on operators gradually became more and more radical. Instead of limiting their operative procedures to the antrum alone, the adjacent mastoid cells were explored for evidences of disease. It remained for Gruening, of New York, however, to first thoroughly formulate the technique of an operation which had for its purpose the removal of

[1] Read before the Southern Section, American Laryngological, Rhinological, and Otological Society, February 3, 1902.

[2] Archiv für Ohrenheilk., vol. vii. p. 157.

practically all of the cellular structures of the mastoid and the eradication of all foci of diseased bone. Gruening laid particular stress upon the removal of the mastoid tip, thus evacuating the inflammatory products from a few large cells so frequently located in this region.

If one cares to consult the statistics of the fatality of middle-ear suppuration complicated by mastoid involvement, it is surprising how the number of fatal cases has diminished within the last decade. Coincident with this change it will be found that the number of cases operated upon has steadily increased. In other words, it has been conclusively proven that early and prompt operation constitutes the only safe method of dealing with the severer forms of middle-ear inflammation—that is, those complicated by involvement of the bony structures adjacent to the tympanum. As soon as the surgeon became bold enough to perform a complete and thorough mastoid operation it was found that many of the accidents so much feared when the operation was less completely performed practically did not occur. At the time when the mastoid operation consisted simply in perforating the cortex over the region of the antrum by means of a drill, one of the most grave casualties which could occur was the accidental wounding of the lateral sinus. This was always looked upon as an injury of great severity, and one which was not infrequently followed by fatal results. When the more complete operation of removal of the entire mastoid cortex came into vogue it was found that the lateral sinus was not infrequently exposed for a considerable portion of its length, and that the favorable outcome of the case was in no way affected by even extensive exposure of this large venous channel. It was also found that even the accidental wounding of the lateral sinus was not followed by any grave symptoms. It became evident that the previous fatal cases ascribed to this accident were due to the fact that it was necessary to stop the operation before evacuating the purulent focus within the bone. With a small opening it was practically impossible to control the hemorrhage from the sinus, and the operation had to be stopped immediately. With the mastoid cortex entirely removed the hemorrhage could easily be controlled by pressure, the operation could be proceeded with, the purulent collection evacuated, and the patient entirely relieved. Gradually the operator became more daring, and when the lateral sinus was exposed during the course of the operation it was carefully inspected and examined for any evidences of infection having extended into this region. This was especially true in those cases where the temperature of the patient seemed to indicate severe systemic infection. When the sinus was found to contain a thrombus partially or completely filling its lumen, the next step was to turn out this clot, to thoroughly curette the sinus wall to remove any possible source of systemic infection, and to then control the hemorrhage by means of a firm, aseptic packing.

This procedure has been followed by excellent results. It was found, however, that in spite of such radical interference in the immediate neighborhood of the mastoid region a large proportion of cases of invasion of the lateral sinus terminated fatally or only recovered after suffering from a severe general pyæmia. A study of these cases led Ballance[1] to institute a procedure of the greatest importance in aural surgery. Realizing that the direct avenue of infection from the breaking down of thrombus in the lateral sinus was through the internal jugular vein, Ballance proposed and successfully carried out the procedure of ligating the internal jugular in the neck, so as to completely shut out any infection through this channel. Following out this plan of treatment, some surgeons were contented to simply ligate the internal jugular; others divided the vessel between two ligatures, and then attempted to wash out the thrombus by irrigation from the cut end of the jugular up through the sinus wound. A further advance in operative technique led to a ligation of all the tributaries of the internal jugular, and finally to the excision of the internal jugular from a point low down in the neck to a point just below the entrance of the vein into the base of the skull, all tributary branches being tied off. This latter procedure seems to be the one of election at the present day.

It is a matter of great importance to the otologist to know in exactly what cases a simple freeing of the lateral sinus from the infective thrombus will be sufficient to prevent systemic infection, and, on the other hand, in what cases it will be necessary to perform the more radical operation of excision of the internal jugular vein. The statistics of cases operated upon within the last decade have been thoroughly collated by Koerner[2] and Hessler.[3]

Koerner (page 72) has reported 20 cases operated upon, in 8 of which the internal jugular was not ligated. Of these 8 cases, 4 recovered and 4 died. In 12 cases the jugular was ligated, and of these 9 recovered.

Hessler[4] reports 54 cases of sinus phlebitis treated by opening the sinus. Of these, 31 cases have recovered and 23 died. In 23 cases the jugular vein was either ligated or opened throughout its entire extent. Of these, 16 recovered and 7 died. In 4 cases where the treatment consisted simply in ligation of the internal jugular, 2 recovered and 2 died.

The statistics of both these authors would seem to indicate the advisability of either resection of the internal jugular vein or, in cases where this was impossible, of dividing it low down in the neck, between two ligatures, opening the vein throughout its entire extent and packing the cavity with iodoform gauze, in order to prevent purulent infection.

[1] Lancet, May 17, 1890.
[2] Die Otitischen Erkrankungen des Hirns der Hirnhäute und der Blutleiter, 1894.
[3] Die Otogene Pyämie, 1896.
[4] Loc. cit., p. 461.

I am convinced, however, that statistics of this kind are apt to be misleading. During the last few years I have operated upon 22 cases with sinus thrombosis. Of these 22 cases 2 have died, one of septic pneumonia, without any evidence at any time that the internal jugular vein was involved; the other of an acute nephritis, apparently induced by the administration of ether. In 4 of these cases only was it found necessary to ligate the internal jugular vein, and in all of these 4 cases recovery took place. In addition to these cases I have reported a fifth case of septic thrombosis of the internal jugular following a middle ear operation for a chronic suppurative otitis media. In this case the internal jugular was also excised, and the patient made a complete recovery.[1]

From these statistics it will be seen that from a relatively large number of cases of thrombosis of the sinus operated upon without interference with the internal jugular vein, the proportion of recoveries is exceedingly large and much in excess of those reported by either Koerner or Hessler; while in those cases in which the internal jugular has been excised in no single instance has death followed. In the one case in which death might possibly have been due to septic infection—that is, in which the patient died of pneumonia—it is quite possible that the pulmonary infection was tubercular in character, although bacteriological examination failed to confirm this view. The temperature chart was certainly not one characteristic of septic infection.

The question of practical moment to the surgeon and to the otologist is, then, How shall we differentiate between these cases? My own experience has led me to believe that prompt operative interference of the most radical kind is the only plan which promises safety to the patient. Cases of middle ear suppuration daily come under observation, especially in dispensary practice, with an exceedingly obscure and imperfect history. Many times it is impossible to keep the patient under observation for even twenty-four hours before operation. The indications for immediate operation upon the mastoid being imperative, there is no opportunity to observe the general condition of the patient or to make note of those variations in temperature which are so characteristic of infection of the lateral sinus and of a dissemination of this infection through the general circulation. My experience has been that the surgeon must decide during the primary operation what course he will pursue. It has been my invariable practice during the last five or six years whenever I have performed a mastoid operation to remove thoroughly all evidences of carious bone, and to follow the softened bone to the dura in every direction, if this is necessary for the complete eradication of the infected areas. When the lateral sinus is exposed,

[1] Archives of Otology, vol. xxvii. p. 297.

unless this vessel appears perfectly healthy on palpation, and unless the external surface is white and glistening and the vessel seems to be of normal size, it is my invariable practice to incise the sinus wall for exploratory purposes. I was formerly in the habit of exploring the sinus by the introduction of a large aspirating needle. I soon found, however, that in some instances where infection of the sinus had taken place, and where a clot was present, the exploring needle withdrew fluid blood. I have, therefore, within the last few years abandoned this procedure entirely; and in every case where I am in doubt as to whether or not the sinus is normal I have made a free incision through the sinus wall. It goes without saying that previous to this exploratory incision every purulent focus must have been removed from the mastoid process—that is, the mastoid antrum must have been thoroughly cleaned out and all pneumatic spaces must have been broken down and curetted, so as to avoid any possible infection of the sinus as the result of the exploratory opening. After this has been done it has been my practice to pack off the antrum by means of iodoform gauze and to thoroughly cleanse the entire field of operation before opening the sinus. All instruments are also carefully re-sterilized before this exploratory incision is made. Before making an exploratory incision into the sinus wall it must be borne in mind that the sinus must be exposed by removing the bony covering of the sigmoid groove for a distance of at least three-quarters of an inch. Pressure is then applied to the sinus above, and the sinus wall is incised close to the knee by means of a sharp, straight bistoury. This incision should lie at about the middle of the area of sinus exposure. If there is a clot in the sinus at this point there will either be no hemorrhage at all or a very slight hemorrhage from below. A curette is then passed into the lumen of the sinus and the clot removed, so that free bleeding is established from below. Pressure is now applied at the point of incision in the sinus and the pressure above is removed. If free hemorrhage does not occur from the direction of the torcular a curette is introduced in this direction, and the lumen of the vessel thoroughly curetted until free hemorrhage is established, it being imperative that free hemorrhage be established from the upper end of the sinus, excepting in those cases where the lumen of the vessel is occluded by a firm fibrinous clot which has evidently been in position for a long time and has become thoroughly organized. Where such a condition is found, and where the lumen of the vessel seems to be obliterated and the entire vessel has been converted into a mass of connective tissue, it is then unwise to attempt to break down this firm plug in the upper portion of the sinus. Naturally, if the clot has become firmly organized no further infection can result from it. Where free hemorrhage is established both from the upper and lower angles of the sinus wound, or where the upper portion

of the vessel seems to be firmly occluded by an organized clot and there is moderate bleeding from the lower angle of the wound, I do not deem it advisable to institute a more radical procedure at the time of the primary operation. Hemorrhage should be controlled by firmly packing the sinus wound by means of iodoform gauze, and shutting off the sinus area from the middle ear and adjacent mastoid cells by means of a firm packing of iodoform gauze. Such a dressing will remain in position for from four to six days, and there is no indication for its removal unless there is a sudden rise of temperature to 103° to 104° F.

If all suspicious cases are treated in this manner at the time of primary operation, and if, whenever there is any doubt as to a possible involvement of the sinus, this vessel is opened for the purpose of exploration simply, I can say, as the result of a rather long experience, that no possible unfavorable issue is to be expected. On the other hand, if, after a period of from one to three days, the temperature shows any indication of systemic infection, I have always found it advisable to proceed immediately to prevent absorption of the poison by means of excision of the internal jugular vein.

In two cases already reported[1] and in two to be mentioned later this necessity arose; and in another case[2] where primary infection of the internal jugular occurred as the result of a middle ear operation this same plan was followed. In all of these cases the temperature fell immediately after the operation upon the middle ear or mastoid, but in the course of a few hours showed those marked remissions characteristic of pyæmic infection.

In these cases my procedure has been as follows: The internal jugular vein was exposed throughout its entire length by means of an incision extending from the sternal attachment of the sternomastoid muscle to the tip of the mastoid process. Owing to the ease with which the internal jugular is exposed low down in the neck, the vessel was in every instance dissected from its sheath first in this region, surrounded by two ligatures, and divided between them. The distal end of the vein was then clamped with an artery clamp, and being raised by an assistant was rapidly dissected upward until the common trunk of the temporal and facial was reached. This trunk was surrounded by two ligatures and divided between them. Occasionally the thyroid veins were large enough to demand attention, and they were treated in exactly the same manner as the common trunk of the temporal and facial. There is also found at times a branch of communication between the external and internal jugular. Where this vessel is large enough to occasion free hemorrhage after its division it should be surrounded by two ligatures and divided between them. In this way the entire trunk of the jugular

[1] Loc. cit., vol. xxix. p. 472.

[2] Loc. cit., p. 471.

is dissected out from its position from a point just above the clavicle to a point just below the base of the skull, the vein being followed as high up as is possible. At the uppermost point of dissection two ligatures are again thrown around the trunk of the vein and the vessel is divided between them. In this way any systemic infection is practically prevented. The lateral sinus having been freed of all infectious material from above, and the jugular trunk having been removed in its entirety from below, there only remains a small portion of the sinus occupying the jugular fossa, and commonly known as the jugular bulb, which can be a source of infection. Simple cleansing by means of irrigation through the sinus wound will effectually free the jugular bulb from any infectious material.

In cases where the infection of the vein has existed for some time, or where the process has been very rapid, the tissues may be found to be so matted together about the vein as to preclude the possibility of a complete dissection of the internal jugular.

I reported such a case in the *Archives of Otology*, vol. xxix. p. 472, in which the disintegration of the walls of the vessel had been so extensive that the vein could only be secured by pulling it forcibly upward from beneath the clavicle. The tributary vessels were so much involved that it was only possible to tie them by means of including a considerable amount of the adjacent muscular tissue and fascia between the ligatures. In this instance it was, however, decided to pass two ligatures about the vein, close to the base of the skull, and to divide the vessel between these two ligatures. In this way the infective focus was cut off from the general circulation, the entire wound was packed with iodoform gauze, and the vein left *in situ*. Complete recovery followed operation.

In addition to the three cases of thrombosis of the internal jugular already mentioned, two others have come under my observation during the last year which it is perhaps worth while to report somewhat in detail:

Case I.—Male, aged thirty-one years, who came to the hospital with the characteristic symptoms of an acute mastoiditis. Under ether the mastoid was opened in the typical manner by one of my colleagues. Owing to a malposition of the lateral sinus, the sinus was entered either by the gouge, or, as I believe more likely, the internal table had already become carious, and on removal of a spicula of bone which was adherent to the sinus the necrotic wall of the vessel was ruptured; at any rate, quite free hemorrhage followed. I then took charge of the case, and succeeded in controlling the hemorrhage and opening the mastoid antrum. I exposed the lateral sinus for a distance of about three-quarters of an inch, and incised the wall in the manner already described. The sinus was not perfectly normal, and there was a small parietal clot. The wound was packed in the manner detailed above and the patient returned to bed. The temperature steadily rose until, on the day following the operation, it was 104.5° F. This eleva-

tion continued for two days. On the fourth day after operation the temperature reached 104.8° F., and the patient was drowsy. Although this persistent temperature elevation was not what would be expected as the result of thrombosis of the lateral sinus, I deemed it advisable, on account of the hemorrhage from the sinus at the time of the operation and from the fact that it was possible that all infective material had not been removed from the cavity of the vessel, to prevent any possibility of systemic infection by ligation of the internal jugular. The vein was therefore exposed in the neck, in the manner already described, and was thoroughly dissected out from a point just above the clavicle to a point just below the base of the skull, all tributaries being divided between two ligatures. During the course of the operation the internal jugular was wounded, and the patient lost considerable blood. The vein contained fluid blood throughout its entire extent, although it seemed to be slightly narrowed at a point just below the base of the skull. Owing to the loss of blood at the time of operation, the patient did not rally for about thirty-six hours. At the end of this time, however, the temperature had dropped slowly, and meantime the condition of the patient had improved decidedly. Although the wound in the neck had been sutured, infection occurred, and the wound healed by granulation. During the period of convalescence the patient developed a mild rheumatic inflammation of both shoulder-joints. At no time, however, did this seem to be septic in character. The patient made a complete recovery, and when seen nine months after the operation was entirely well.

This case, I think, demonstrates rather clearly the necessity of prompt operative interference, having for its purpose the cutting off of all circulation through the affected side in case the temperature after primary operation upon the sinus remains high.

Another case operated upon a few weeks ago bears out this point.

CASE II.—The patient, a male, aged eight years, was admitted to the hospital with the history of having had a purulent discharge from the right ear for about six years. For a week there had been pain in the ear, and for three or four days the patient had been feverish and somewhat chilly. On examination it was found that there was a subperiosteal abscess behind the ear. This was evacuated by operation and the cavity of the abscess curetted. On exposing the mastoid cortex this was found to be perforated in several places. The cortex of the mastoid was removed, and the interior was found to be filled with pus and granulation tissue. The bony wall of the sinus was destroyed, and the lateral sinus was bathed in pus. The sinus wall was protected by a pad of iodoform gauze; the antrum was thoroughly curetted and all necrotic tissue entirely removed. During this procedure the dura was exposed in the region of the tegmen tympani over a small area. The antrum was now packed with iodoform gauze, and the sinus was further exposed from the knee to a point just above the bulb. The wall of the sinus was incised, and this incision was followed by no bleeding, the sinus being filled by a clot which completely occluded its lumen. An attempt was made to remove this clot by means of a curette introduced into the sinus and passed downward toward the bulb. The clot was found to be fairly firm, and absolutely no hemorrhage followed the use of the curette.

The curette was next introduced into the sinus in the direction of the torcular, and free hemorrhage was established. The sinus was plugged in this region, and, owing to the fact that the clot was soft and that the lower end of the sinus could not be made perfectly patent, it was deemed advisable to proceed at once to excision of the jugular vein. This was accomplished in the manner already described. When the ligature was placed about the vein close to the base of the skull the pressure of the ligature severed the vessel completely. No hemorrhage followed. The external wound in the neck was sutured for three-quarters of its length, the wound being left open at the upper angle, where a packing of iodoform gauze was carried inward into the jugular fossa. The patient was returned to bed, and the first dressing was changed on the fourth day. The temperature had remained normal up to this time. After this the dressing was changed either every day or every alternate day until the twelfth day, when a slight elevation of temperature was noticed. The temperature was not high, but would vary between normal in the morning to 101° to 101.5° F. in the afternoon. This continued for about three days, in spite of daily dressings. At this time I dressed the case myself, and, upon the introduction of a director into the lower angle of the sinus wound, found a considerable collection of pus in the jugular bulb. The probe introduced into the wound in the neck at the point where the jugular had been divided also evacuated about 10 minims of pus. Both the lower sinus wound and the wound in the neck were thoroughly irrigated with a solution of bichloride of mercury of a strength of 1 : 5000, and both wounds were thoroughly packed with iodoform gauze. After this there was no further rise in the temperature, and the patient made an uneventful recovery. The wound in the neck did not unite by first intention, but healed by granulation. A bacteriological examination of the clot removed from the sinus showed a few streptococci. Careful inspection of the vein, however, at its upper portion showed absolutely nothing abnormal. In spite of this fact the temperature fell immediately after operation, and continued to remain normal until incomplete drainage caused a slight temporary temperature elevation.

This case seems to show the advisability of prompt operative interference in cases where the history is uncertain and where a clot is found to occlude the lower portion of the sinus. I do not say that this means that this case might not have recovered had not the jugular been interfered with. In view of the fact, however, that even after a complete cutting off of the purulent focus from the general circulation the comparatively small amount of pus retained in the bulb was sufficient to give rise to marked temperature changes, I feel convinced that had the jugular at that time been in position, thus affording an avenue of entrance for the purulent germs to the general circulation, the termination of the case would certainly have been fatal.

It seems to me wise, therefore, in all doubtful cases, to remove the internal jugular vein in order to eliminate this element of doubt in the case. I would not be misunderstood in this statement. I do not advise that in every instance of sinus thrombosis the internal jugular

be interfered with. I believe that where the patient has been under observation for a few days, and where we have a fairly complete temperature record of from twenty-four to forty-eight hours, showing no marked evidences of systemic infection, the surgeon may rely upon simply clearing out the clot in the sinus, if this be found. I believe that this same procedure should be followed in cases which first come under observation at the time of operation and in which the surgeon is able to clear the sinus fairly well of the clot by means of the curette. On the other hand, those cases which are first seen at the time of operation, and in which the sinus cannot be thoroughly cleared, and in which also the surgeon is confident that a certain amount of infected material is left in this venous channel, demand, I believe, immediate excision of the internal jugular vein. The operation is in no way a serious one, and, as it consumes but little time, does not endanger the patient by prolonging materially the period of anæsthesia, while, at the same time, it prevents any possibility of further systemic infection. I also believe that in those cases where after primary operation in which the sinus has been cleared as freely as possible, and where, in spite of this, at the end of forty-eight or seventy-two hours evidences of systemic infection are still present, the surgeon should not delay further operative interference—that is, he should immediately proceed to the excision of the internal jugular vein.

In deciding upon the advisability in the cases last mentioned I believe that the temperature chart is the only sure and certain guide. Much has been said by various authors about tenderness in the neck over the region of the jugular. This may be present, or it may be absent. Even in the absence of any such tenderness, with a remittent temperature which is gradually becoming higher and higher, and with a certain knowledge that the lateral sinus is already infected, I believe that the surgeon errs on the side of conservatism who longer delays operative interference.

HEMIHYPERTONIA POSTAPOPLECTICA, WITH SOME REMARKS ON A CONTRALATERAL ACCESSORY MOTOR SPEECH CENTRE.[1]

By D. J. McCarthy, M.D.,
OF PHILADELPHIA,
ASSOCIATE IN THE WILLIAM PEPPER CLINICAL LABORATORY, UNIVERSITY OF PENNSYLVANIA; INSTRUCTOR IN NERVOUS DISEASES, PHILADELPHIA POLYCLINIC; VISITING PHYSICIAN TO THE PHILADELPHIA HOME FOR INCURABLES, ETC.

V. Bechterew[2] reported three cases of a condition to which he gave the name hemitonia apoplectica. Spiller,[3] shortly after the appearance

[1] Presented at the November meeting of the Philadelphia Neurological Society.
[2] Deutsche Zeitschrift für Nervenheilk., 1900.
[3] Philadelphia Med. Journ., 1899.

of this paper, read a paper on the subject, and suggested the name "hemihypertonia postapoplectica." The case here reported is the only case, other than that presented in Spiller's paper, reported in this country. One other case has been reported in the German literature.

The condition as described by v. Bechterew is one of intermittent tonic spasm distributed over one-half of the body, affecting at times different groups of muscles, without loss of power in the muscles affected, and follows an apoplectic attack. He reports in his paper three cases. In all three cases the initial lesion occurred in early life—before the tenth year. This was also true of Spiller's case. In two of the three cases the apoplectic attack followed some infection. The clinical course of the three cases and the other cases reported varies considerably. The apoplectic attack lasted a few minutes in one of v. Bechterew's cases, and in another continued over a period of five days. In Pfeiffer's[1] and in my case there was no unconscious period at all. The development of the spasm and the degree of paralysis differs in different cases. The spasm may develop immediately after the apoplectic attack or initial symptom group, or may be deferred months or even a period of two years, as in the case reported in this paper. The loss of motor power may vary from a distinct hemiplegic weakness to cases in which there is no appreciable loss of power. After a varying interval of time following the cerebral disturbance certain groups of muscles on one side of the body (the arm, leg, and face are usually affected) go into a condition of hypertonicity. A slight irritation, such as a pin-prick or rough handling, is sufficient to throw these muscles into a tetanic spasm. After a few seconds or minutes the spasm passes from the flexor groups to the extensor groups of muscles, and then disappears. In some cases there may be repeated alternations of these flexor and extensor spasms, and as each repeated spasm is associated with a corresponding flexor or extensor movement the result might be mistaken for athetosis. The spasmodic condition of the muscles is somewhat relieved by distracting the patient's attention or by light rubbing of the part. In one of the cases the spasm disappeared during sleep; in two other cases a tenseness of the muscles persisted during sleep. The deep reflexes and the muscle irritability are usually increased.

The main features in the case about to be described are: 1. The presence of an attack of dizziness, associated with numbness in the left arm, and aphasia lasting twenty minutes. 2. An attack of vertigo in 1898, following which she had severe occipital headaches for a period of about a year. 3. The development, almost a year after the second attack of vertigo (fall of 1900), of intermittent, alternating flexor and extensor spasms affecting the left lower leg and arm, associated with

[1] Neurologisches Centralblatt, 1901.

a very pronounced increase of the muscle irritability and the knee-jerks. The detailed history is as follows:

M. D., aged forty-seven years, single, female, dressmaker by occupation, came to the clinic complaining of nervousness resulting from spasm of her foot and hand. Her father had died of a paralytic stroke. There was no other nervous affection in her family. She had had the usual diseases of childhood, followed by typhoid at ten years of age. She had a second attack of typhoid at the thirtieth year. She was in fairly good health from that time until the fall of 1898.

FIG. 1.

FIG. 2.

Present History. In the fall of 1898, while at work, an attack of dizziness occurred, which lasted twenty minutes. During that time her tongue was so thick that she was unable to talk. There was numbness in the left arm and face. The left arm was weak, but she could still move it. The left face drooped, and a physician who saw her in the attack said she had a slight stroke. All the symptoms passed off with the dizziness at the end of twenty minutes. There was no loss of consciousness. In the fall of the following year another attack of dizziness occurred. Objects in front of her swayed from one side to the other. She sank slowly and easily to the floor, to prevent herself from falling. There was no unconsciousness with this attack, nor were there any of the symptoms noted in the previous attack. For a period of about a year following this attack she was troubled with severe occipital head-

aches. There has been no vomiting or other symptoms of intracranial pressure.

In the fall of 1900 the spasm of the foot began to develop. She first noticed that at times, when walking, the middle toe of the left foot would become contracted and prevent her from walking until she rested for a time and gave the part a chance to recover its normal condition. Since that time this condition has gradually grown worse, until now all the toes, the lower leg muscle groups, and to a slight extent the upper leg groups, are affected. Any rough handling or irritation or an attempt to elicit the plantar reflex will bring on a tonic flexor spasm of the smaller toes (see Fig. 1) and an extensor spasm of the great toe, which after several minutes may change to an extensor spasm of all the toes or disappear without any extensor spasm. During the spasm of the toes the calf muscles are hard and rigid. There is a considerable degree of hypertrophy of the muscle groups affected. The hand is held in a position of flexion, with the thumb drawn in toward the palm. (See Fig. 2.) There is always an increased tonus in the hand and arm muscles, and at times the condition of flexor tetanic spasm is very similar to that seen in tetany. The spasm of the leg or arm muscles occurred usually only at long intervals. In walking a hundred yards the patient was compelled to stop four times on account of the spasm in the foot.

There is no appreciable weakness either in the arm or the leg. The dynamometer: Right side, 70; left hand, 65. The tongue deviates constantly to the left. Pupils are equal, eye reflexes normal, fundi normal. Knee-jerk: left, increased; right, increased. Achilles jerk: left, normal; right, absent. Plantar reflex: left, difficult to determine, on account of spasm; right, absent. Biceps jerk: left, present, increased; right, present. Triceps jerk: left, present, increased; right, present. Chin jerk: left, present; right, present. Supraorbital reflex: left, increased; right, present.

The muscle irritability to mechanical irritation was very markedly increased in all the muscle groups of the left arm and leg, and to a lesser degree on the right side of the body. Sensation is normal. There is no astereognosis.

A fact of considerable importance in the history is that she has used the left hand since early childhood much more than the right, although she writes with the right hand. It would therefore appear from the symptoms presented in this case—such as the temporary aphasia, with persistent deviation of the tongue, for several years, and temporary loss of power in the right arm—that in the original cerebral lesion the speech fibres were affected. The rapid recovery of the function of speech in the presence of the paralysis of the tongue could be explained in this case, and in another case of persistent and complete hemiplegia in a left-handed person who later learned to use the right hand for writing purposes, and in whom the loss of speech lasted several weeks after the apoplectic attack, by assuming that in such cases there is a fairly well-developed speech centre in both hemispheres. The original speech centre evidently is the main centre, because in the hemiplegic case the patient was aphasic for several weeks after a

right-sided lesion; and what might be termed the accessory contralateral motor speech centre, developed coincidentally with the education of the hand in writing movements, takes up the function of speech under such conditions only after some additional training and considerable effort on the part of the afflicted individual.

The absence of any period of unconsciousness in the case of hypertonia here reported is of considerable importance. The name suggested for this condition by v. Bechterew and the modification suggested by Spiller both assume an apoplectic attack, which if restricted to its exact meaning would necessarily imply an unconscious period.

The absence of any marked weakness other than that of the tongue is sufficient to differentiate it from other postapoplectic conditions, such as athetosis, chorea, tremor, contracture, etc. The almost if not complete absence of paralysis in this case should stamp it as the most typical example of this affection on record. The case is somewhat different from those described by v. Bechterew in the absence of this initial unconscious period and in the long period intervening between the cerebral insult and the development of the hypertonia. There has as yet been no autopsy in a case of hypertonia apoplectica. The determination of the nature and character of the lesion and its position must, therefore, be open to discussion until such an autopsy occurs. v. Bechterew holds that the lesion is not cortical, on account of the absence of clonic convulsive movements; that it is not subcortical, on account of the wide extent of the peripheral manifestations necessitating an equally wide-spread lesion in the subcortex; and that it is probably a lesion of the basal ganglia in the neighborhood of the posterior limb of the internal capsule. The symptoms can best be explained, he thinks, by a small lesion causing direct irritation of the motor tracts or secondary irritation through the tension of a healing cicatrix. This case is reported from the clinic of Dr. Spiller at the Philadelphia Polyclinic.

THE ETIOLOGY OF INFANTILE PARALYSIS.

By Alfred M. Gossage, M.B. Oxon., M.R.C.P.,
ASSISTANT PHYSICIAN TO WESTMINSTER HOSPITAL AND TO THE EAST LONDON HOSPITAL FOR CHILDREN.

Much discussion has arisen as to the causation of the disease known as infantile paralysis, but the question is still far from being settled. Our knowledge as to its nature, derived from its clinical aspects and from a careful examination after death of the bodies of its victims, is assisted by the flood of light which recent research has shed on the anatomy, physiology, and pathology of the muscular and nervous sys-

tems. Infantile paralysis is characterized by a loss of muscular power in one or more limbs of acute onset, followed by more or less muscular wasting. We now know that muscle fibres depend for their nutrition on their connection with certain cells in the spinal cord by means of the nerve fibres that supply them, so that destruction of the nerve cell involves destruction of the nerve fibre and its attached muscle fibre. Disease and destruction of the muscle or nerve fibre do not necessarily, however, bring in their train death of the nerve cell; indeed, the nerve fibre may be regenerated by a fresh outgrowth from the nerve cell and form a fresh attachment to the muscle fibre.

Paralysis and degeneration of the muscle fibres may be due to a primary disease of the muscle, the nerve to the muscle, or the cell of which that nerve is a process. Primary disease of muscle fibres is usually chronic in its course, and since it is generally hereditary, is probably due to some congenital defect. Occasionally, it is true, acute degeneration of muscle fibres does take place in certain specific fevers, probably from the action of some toxin. Hence an acute destruction of muscle fibres is more commonly due to some disease either of its nerve fibre or of the nerve cell from which that fibre is derived. The nerve cell and fibre[1] may be attacked separately or together, and the resulting disease may be acute or chronic in its course. Destruction of the nerve fibre does not necessarily mean a permanent wasting of the muscle fibre, since a fresh connection may be established between the nerve cell and the muscle, while destruction of nerve cells, since they are never replaced, always involves the complete degeneration of their muscle fibres. A local injury may separate the nerve cell from the muscle by severing the nerve fibre or may destroy the nerve cell itself. Inflammatory processes may involve the nerve cell or fibre, and so may temporarily or permanently render them useless, and their functions may similarly be temporarily or permanently abolished by some lesion that cuts off their blood-supply. Lastly, the nerve cell or fibre may be acutely disabled by the action of some poison circulating in the blood, and it is possible that such a poison would either only temporarily impair their functions or so seriously damage them that recovery would be impossible. It has been shown during the last forty years that the muscular weakness and wasting of infantile palsy are always due to destruction of the nerve cells in the ventral horns of the spinal cord. Widely different views have, however, been expressed as to how and why the cells are attacked. Clinically there would seem to be more than one disease grouped together under the same name, while the pathologists have regarded the disease as single and due to a single cause. In attempting to ascertain the nature of the complaint it is

[1] Strümpell and Bartholmes. Deut. Ztscht. f. Nervheilk., 1900, xviii. p. 304.

essential to give due weight to both the clinical and pathological evidence.

Clinically there are certain features of the disease which may be considered first. It attacks the very young by preference, being almost confined to the first four years of life, and comparatively rare after the third year. Cases do occur in adult life, but are very infrequent. The disease has a seasonal predilection, being most frequently met with in the hot weather, *e. g.*, the months of July, August, and September. It does not tend apparently to specially attack weakly children, the robust, well-nourished infant being as liable to be affected as one that is feeble and wasted. There does seem, however, to be a special liability to attack in children who have recently suffered from the acute specific fevers of childhood, measles, scarlet fever, and diphtheria.[1] The paralysis is at its maximum in extent within a short time of the onset, and is almost invariably much more extensive at first than it is later on. Recovery of power starts almost at once and progresses gradually over several months; complete recovery, however, does not take place, or, in other words, some of the motor cells are always destroyed.[2] The permanent paralysis may be limited to a single limb or to a single group of muscles, or even a single muscle, although at first all the limbs may have been nearly powerless. The lower limbs are attacked much more frequently than the upper. Following on the local paralysis, local deformities frequently develop, owing to the unopposed action of the healthy muscles. When there has been extensive paralysis of one limb it is usually colder than its fellow, and there is a general want of development, so that the bones in the paralyzed limb are smaller and shorter than in the healthy one. The loss of power in the permanently paralyzed muscle fibres is absolute from the first, and there is a rapid loss of electrical excitability, as rapid as when the nerve to the muscle is cut. In muscles that are about to recover, the loss of power is either not quite absolute or is only absolute for a very short time. The electrical excitability of these muscles is, too, never quite lost, there being always some reaction to the galvanic current. As in other cord diseases, an acute arthritis sometimes occurs which may be mistaken for acute rheumatism.[3]

Although nearly all cases of infantile paralysis conform to the description given above, they differ markedly from one another in their clinical aspect during the first few days. One may, indeed, divide them into classes according to these initial symptoms. The most striking cases, although not the most numerous, are those in which a child without any other sign of ill-health becomes suddenly paralyzed. On

[1] Zappert. Jahrb. f. Kinderheilk., liii. Gowers. Diseases of Nervous System, vol. i. p. 353.
[2] Pasteur's cases, given below.
[3] Coutts. Medical Times and Gazette, 1885, p. 76. Barlow. British Medical Association, 1888.

awakening it in the morning the mother may find it unable to move one or more limbs, or the onset may be even more sudden than this, the child tripping or falling in walking or running, and when picked up being found paralyzed in one leg. This sudden loss of power is unaccompanied by any pain or sign of the patient not being perfectly well, and there is not the slightest alteration of sensation to be found. Such a sudden onset is more common in young children, under the age of two years. According to Coutts,[1] in cases which have commenced in this sudden fashion, the initial palsy is usually limited to one limb, and the ultimate persistent paralysis is confined to a few muscles in that limb.

Case I.—Maud R., aged two years, was found by her mother one morning to have lost the use of the right arm, having been perfectly well the night before. On examination there was flaccid paralysis of all the muscles of the right arm and shoulder; some slight movement of fingers. No other limbs affected.

In another class may be put the more common type of case where there is a good deal of fever and malaise and frequently vomiting for some hours or even a day or two before the onset of the paralysis. The amount of the early loss of power is usually wide-spread, both lower limbs, and both upper limbs and trunk being affected. The permanent paralysis, too, is frequently very extensive. The full extent of the paralysis may appear suddenly, or it may require some hours or even days to develop. Pain and tenderness in the affected limbs are not uncommon symptoms, but no other affection of sensibility seems to occur. As a type of this class one may record the following case:

Case II.—E. P., aged five years, a bright, lively girl, was noticed to have lost her appetite at supper one night. She vomited after supper and several times during the night. Next day she was found to be unable to stand or even to sit up, and she complained of considerable pain in the back. On admission to the hospital there was flaccid paralysis of all limbs, absence of knee-jerks and superficial reflexes; no anæsthesia and no loss of control over rectal and vesical sphincters or paralysis of cranial nerves. After admission she gradually recovered power to some extent in all muscles except the right deltoid, and at the end of three months could raise herself to a sitting position and could walk with the help of her arms. On discharge from the hospital there was permanent complete paralysis of the right deltoid and partial paralysis of all the muscles of both legs.

The disease is uncommon in adults, but such cases as do occur nearly always resemble that more common type in children which has been last described. Pain in the back and limbs are very prominent symptoms, much more so than in children, and the onset of the paralysis is

[1] Private communication to author. Gowers. Diseases of Nervous System, vol. i. p. 357.

much less rapid. The case reported by Williamson[1] may be taken as an example, especially as the clinical diagnosis was confirmed post-mortem.

CASE III.—A man, aged twenty-two years, was attacked with pain in the back, slight pain in the limbs, and at the same time a numb feeling was noticed in the right hand. On the next day there was numbness in the right leg and to a less extent in the limbs on the opposite side. The patient also noticed that the right arm was weak, and this weakness rapidly increased so that the right arm became completely paralyzed, and later the right leg also. On the third day the limbs of the left side became completely paralyzed. The bladder and rectum were not affected, and there was no anæsthesia. Slight improvement began after ten days, and the patient became able to just move his arms and toes. After being ill for five weeks he one day died quite suddenly. At the post-mortem examination an inflammatory condition was found in the ventral horns of the spinal cord similar to that described later on.

Very few opportunities have occurred for the examination of these adult cases post-mortem. But besides Williamson's case, a few others have been reported.[2]

Cases of infantile palsy generally occur sporadically, and beyond the seasonal prevalence no connection between any two individual cases can, as a rule, be found, but sometimes two or more children of a family are attacked soon after one another. More rarely a large number of cases arise in a small district within a short time, thus constituting a veritable epidemic. In such an epidemic in Vermont, reported by Caverly,[3] as many as 140 cases occurred. The clinical symptoms in these epidemic cases resemble the more common type of the sporadic cases, *i. e.*, the cases occur in the summer, there is initial fever and malaise, with headache, pain in the back, and vomiting, and then, after a day or two, loss of power comes on more or less suddenly. There are, however, certain features peculiar to these epidemics. Convulsions and coma are occasional early symptoms, while they are almost unknown in the sporadic cases. Pains in the back and limbs are more severe and more frequent, being almost invariable, and the limb pains may be associated with tenderness over the nerve trunks, and even some anæsthesia in the distribution of the peripheral nerves, showing that there is some accompanying multiple neuritis. Certain cases occurring during the epidemic, and probably arising from the same exciting agent, have

[1] Medical Chronicle, 1890, vol. xii. p. 454.

[2] Schultze. Virch. Archiv, 1878, vol. lxxiii. Leyden. Archiv f. Psychiatrie, 1875, vol. vi. p. 271. Friedländer. Virch. Archiv, 1882, vol. lxxxviii. p. 84.

[3] Caverly. New York Medical Record, 1894, vol. xlvi. p. 671. Cordier. Lyons Médical, 1888. Strümpell. Quoted by Goldscheider, Zeitschft. f. klin. Med., 1893, vol. xxiii. p. 554. Newmark. Med. News, 1899. Packard. Journal of Nervous and Mental Disease, 1899, vol. xxvi. p. 210. Zappert. Jahrb. f. Kinderheilk., vol. liii. Chapin. Archives of Pediatrics, November, 1900. Brackett. Transactions of the American Orthopedic Association, 1898, vol. xi. p. 132.

only the clinical aspect of multiple neuritis without any evidence of implication of the spinal cord at all. For instance, in the epidemic of 44 cases in Stockholm, reported by Medin,[1] there were two cases of simple multiple neuritis besides several mixed cases of anterior poliomyelitis and neuritis. Again, during an epidemic of multiple neuritis in Hamburg, reported by Eisenlohr[2] in 1887, where the illness started with fever, diarrhœa, and vomiting, two cases of anterior poliomyelitis occurred which Eisenlohr considered were due to the same exciting cause as the cases of neuritis. In these epidemics, too, the implication of the cranial nerves, or rather their nuclei, is comparatively frequent. The simultaneous occurrence of anterior poliomyelitis and multiple neuritis in the same patient, and probably due to the same exciting cause, has been noted in sporadic cases by several observers.[3] The association, however, is common in epidemic cases and extremely rare in the sporadic. The implication of the cranial nerves, too, has been observed in sporadic cases, but only in one or two instances.

The disease itself seldom kills in the sporadic cases, only two such deaths having been reported,[4] but a certain proportion of the patients in these epidemics have died. Death in these instances seems to be due to an attack on the respiratory centre in the bulb.[5] We have evidence, too, that the disease in these epidemics may attack the higher cells in the brain or their axis-cylinders, *e. g.*, Caverly reports that rigidity of muscles was not uncommon in the Vermont epidemic (also Pasteur). In some of the epidemics certain patients who are obviously attacked by the prevailing disease may never show more than a slight temporary weakness of certain muscles, or even may show no muscular weakness at all. For instance, in the interesting family epidemic reported by Pasteur,[6] all the seven children were attacked within ten days of one another with fever, backache, and headache; two of these recovered without any sign of muscular weakness, one had some muscular tremor and recovered, one had muscular tremors and transient strabismus, one had ordinary flaccid paralysis of the infantile type, one had some permanent paralysis of the infantile type, but with some initial rigidity, and the last one had hemiplegia with marked rigidity. One must confess, in the light of these cases of Pasteur's, that it is possible that the cause of the ordinary sporadic infantile palsy may produce a febrile complaint, with perhaps temporary weakness, to be

[1] Medin. Verhandlungen des X. Internat. Med. Cong., Berlin, 1890, vol. ii. pt. vi., p. 37.
[2] Eisenlohr. Berlin. klin. Wochenschr., 1887, vol. xxiv. p. 781.
[3] Strümpell, A. Neurolog. Centlblatt., 1884, No. 11, p. 241. Leyden. Archiv. f. Psychiat., 1875, vol. vi. p. 271.
[4] Drummond. Brain, 1885-86, vol. viii. p. 14. Dauber. Deut. Zeitschft. f. Nervheilk., 1893, vol. iv. p. 200.
[5] Medin, Drummond, Dauber.
[6] Pasteur. Clin. Soc. Trans., 1897, vol. xxx. p. 1438.

followed by a complete recovery. We have, however, no further evidence in favor of this hypothesis.

Two cases recently shown to the Neurological Society by Dr. Coutts and myself well illustrate the general aspect of these epidemic cases:

CASE IV.—A brother and sister, aged respectively seven years and five years, were taken to Margate by their parents in the summer of 1899. On the sixth day of their stay, the girl, after a long walk, was attacked with nausea and feverishness, and then several times during the night with vomiting. The following morning she was found to have lost the use of all four limbs and to be unable to sit up. She complained, too, of pain in the back. On this day, August 12th, the family returned to London. On August 16th, the fifth day of the disease, a peculiar gurgling was noticed in the throat, as though the child was going to choke, but this symptom only lasted a short time and did not return. The mother thought that the child improved and regained some little power in both arms during the next four weeks. On September 14th she was admitted to the East London Hospital for Children. She was there found to be a well-nourished child, with the exception that the muscles generally were rather flabby. There was loss of power in all four limbs and she was totally unable to sit up, crying out with pain on any attempt to raise her to a sitting position. The legs could only be drawn up to a very slight extent and she had considerable difficulty in re-extending them, and the knee-jerks were absent. The grasp of both hands was feeble and she was unable to raise either arm from the side. The movements of the palate and eyes were unaffected. She could swallow well, and there was no affection of the sphincters of the bladder and rectum. There was anæsthesia of both legs below the knees. The muscles generally were very tender when grasped, however gently, especially those of the calves, and for a short time there was distinct tenderness over the popliteal nerves. On electrical examination on October 17th only a very slight response could be obtained to both faradism and galvanism in the lower limbs, but in the upper limbs the muscles responded well to both forms of current, with the exception of the right shoulder muscles. The right deltoid did not react to faradism at all, and gave a well-marked reaction of degeneration with galvanism. In the left deltoid the A. C. C. was greater than the K. C. C., but the reactions were otherwise normal. After admission the girl slowly improved, except during an attack of acute pleurisy. The anæsthesia and tenderness disappeared, and there was some general recovery of power, but when she left the hospital, after three months' stay, she was still unable to walk or raise the right arm from the side. During the next twelve months the improvement continued, but a marked lateral curvature of the spine developed, deflection to the right in the mid-thoracic region, possibly due to weakness of the spinal muscles. On examination at the present time, two years and three months from the commencement of the illness, the patient was found to have still further improved. She could walk, though not well, both legs being weak, but especially the right. The muscles of both lower limbs were rather flabby, especially on the right side, and the right leg and thigh were rather smaller than the left; no muscle was, however, completely paralyzed. The knee-jerk could not be obtained on either side. There was marked lateral curvature of the

spine, but even in this some improvement had taken place. Both upper limbs were weak, but the child was capable of performing all movements, and could even raise both arms above the head. The muscles of the right shoulder were apparently a little weaker than those of the left, but none of them were atrophied. The case, therefore, does not now present the clinical aspect of infantile paralysis, and it is quite possible that considerable further improvement may take place in the future. Not improbably the peripheral nerves have here been attacked much more than the cord.

The boy was quite well up to August 17th, but was attacked suddenly the next day, seven days after his sister was first taken ill, with feverishness and loss of power in all limbs, and was unable to sit up. He was admitted to the hospital on September 13th. He was then found to be a well-nourished boy of weak intellect with internal strabismus of both eyes, which had existed from birth. He complained of pain in the back, which was increased upon raising him in bed. There was weakness in all four limbs. He could just walk when supported; the grasps were feeble but equal on both sides; he could just raise the right arm from the bed, but was quite unable to lift the left arm at all. The knee-jerks were absent. There was no anæsthesia, but there was pain on pressure over the nerves of all the limbs and over the left shoulder, although there was no apparent swelling of the joint. During the patient's stay in the hospital he recovered power over all his muscles, except those of the left shoulder, the tenderness disappeared and the knee-jerks returned. The muscles of the left shoulder wasted rapidly and remained quite powerless. The electrical reactions of the muscles were normal except in the muscles of the left shoulder, which reacted only slightly to faradism and gave a well-marked reaction of degeneration to galvanism. At the present time the boy presents a typical picture of infantile paralysis, the left deltoid, supraspinatus, and infraspinatus having completely disappeared.

The amount of evidence that has been afforded us by the examination of patients after death is extremely small. The first to suggest that the disease involved the spinal cord and not the muscles was Heine,[1] in 1840, but it was not until Cornil[2] examined the spinal cords of two cases, in 1863, that there was any definite proof of this. In his cases in which death had occurred, in one a year and the other forty-seven years after the onset, he found that the ventral portion of the cord was smaller than normal, and he considered that the lesion was in the ventral white column. Prévost[3] found in one case atrophy of the ventral horns of the gray matter. It is to Charcot,[4] however, that we are indebted for the knowledge that the disease chiefly attacks the cells in the ventral horns. He examined, with Joffroy, a woman, aged

[1] Heine, J. Beobachtungen über Lahmungszustande der unteren Extremitaten. Stutigart 1840.

[2] Cornil. Compt. Rend. des Seances et mémoires de la Société de Biologie, 1863, series 3, vol. v. p. 187.

[3] Prévost and Vulpian. Ibid., 1865, p. 217.

[4] Charcot and Joffroy. Archives de Physiol. norm. et patholog., 1870, vol. iii. p. 134.

forty-seven years, who in childhood had been attacked with extensive palsy of the lower limbs with resulting permanent paralysis and wasting. They found that the ventral horns in the lumbar enlargement were smaller than normal and that nearly all the cells had disappeared. There was some increase of neuroglia throughout the gray matter, especially in the ventral horns, but the atrophy of the nerve cells was much more conspicuous than the affection of the connective tissues. Charcot considered that the lesion was inflammatory in its nature, but thought that the cells were first attacked and the connective tissues only secondarily.

Roget and Damaschino[1] were able to examine three cases within a few months of the onset of the paralysis, whereas in Charcot's case the disease had existed for many years. In these cases they found marked signs of inflammation which were naturally most marked in the most recent case, where death had taken place two months after onset. There was engorgement of the vessels with much exudation of leucocytes, and in places hemorrhages, and there was also destruction of the cells of the ventral horns with atrophy of the ventral roots, but this destruction was considered by Roger and Damaschino as being secondary to the myelitis and not primary. There followed on the publication of these cases a considerable controversy as to the nature of the pathological process, some upholding Charcot's view, that it was primarily a parenchymatous inflammation of the cells, others the view that the interstitial inflammation was primary, the cells being destroyed by involvement in this.[2]

Leyden,[3] in 1875, from the examination of four cases, in three of which the inflammation seemed to have first affected the connective tissue, in the other the cells suggested that the clinical phenomena of infantile palsy might be caused by two different pathological lesions.

Archambault and Damaschino[4] were the first to describe a really recent case, the previous cases having been attacked many months or years before death. In this instance death took place twenty-six days after the onset of the paralysis. Since that time several still more recent cases have been described, in one of which death took place within six hours of commencement of the illness.[5] In all these the appearances closely resembled those described by Roger and Damaschino, and the authors considered the disease to be an inflammatory myelitis.

[1] Roger and Damaschino. Compt. Rend. des Seances et mémoirs de la Société de Biologie, 1871, p. 49.

[2] Parrot and Joffroy. Archiv. de Physiol. norm. et path., 1870. Roth. Virchow's Archiv, 1873, vol. lviii. p. 263. Schultze. Virchow's Archiv, 1878, vol. lxxiii. p. 443. Charlwood Turner. Path. Soc. Trans., 1879, vol. xxx. p. 202. Taylor, F. Path. Soc. Trans., 1879, vol. xxx. p. 197. Eisenlohr. Deut. Archiv f. klin. Med., 1880, vol. xxvi.

[3] Leyden. Archiv f. Psychiat., 1875, vol. vi. p. 271.

[4] Archambault and Damaschino. Revue mensuelle des Maladies de l'Enfance, 1883, p. 63.

[5] Drummond. Brain, 1885–86, vol. viii. p. 14.

Rissler,[1] who examined four of Medin's cases, three within eight days, and the other seven weeks after the onset, is the only author who has examined recent cases who supports Charcot's view. He found, it is true, hyperæmia and cell infiltration, but considered that the nerve cell degeneration was disproportionately great compared to the amount of interstitial inflammation.

Rissler's views were criticised by Goldscheider,[2] who, from an examination of two cases of his own, one recent and the other of long standing, came to the conclusion that the disease was inflammatory, but primarily occurred in the distribution of the bloodvessels. He pointed out that in most cases, even including Rissler's, the lesion was not confined to the ventral horns, but spread over to the adjacent white columns or to the base of the dorsal horn.[3] The ventral horns receive their blood-supply by the central branches of the anterior spinal artery, and these central branches also supply the adjacent white matter and the base of the dorsal horn. The branches of the central artery course mainly in the long axis of the cord, so that a section of the cord at any level is supplied by branches from several central arteries.[4] Hence, if one such artery escape attack, the cells in its distribution would escape, and so different groups of cells would be affected at different levels. Kawka and Goldscheider have shown by means of serial sections that this is the case. More recently Siemerling, Dauber, and Matthes[5] have found that the disease is inflammatory and that the inflammation occurs only in the distribution of some of the branches of the anterior spinal artery. In recent years von Kahlden[6] has again supported Charcot's original view. von Kahlden's cases were all of long standing—two to sixty years—and so have not the same value for argument as recent cases. He founded his views mainly on the great destruction of nerve cells, with comparatively small signs of inflammation or of destruction of nerve fibres in the ventral horns. While not denying the possibility of a primary atrophy of the cells as a cause for the phenomena of infantile palsy, one may emphasize the fact that the post-mortem evidence is strongly against this view, but it is important to note that the vast majority of recent cases that have come to a post-mortem examination have belonged to the second or more common of the two clinical classes where any account of their onset is given. In

[1] Rissler. Nordiskt. Medicinskt. Archiv, vol. xx. Quoted by Goldscheider.

[2] Goldscheider. Zeitschft. f. klin. Med., 1893, vol. xxiii. p. 494.

[3] Roger and Damaschino. Compt. Rend. de la Soc. Biolog., 1871, p. 49. Roth. Virchow's Archiv, vol. lviii. p. 264. Charlwood Turner. Trans. Path. Soc., 1879, p. 202. Angel Money. Trans. Path. Soc., 1884. Drummond. Brain, 1885–1886, vol. viii. p. 14. Eisenlohr. Deut. Archiv f. klin. Med., 1880, vol. xxvi. Kawka. Inaug. Dissert., Halle, 1889.

[4] Kadyi. Ueber die Blutgefasse des menschliche Ruckenmarkes, Lemberg, 1889.

[5] Siemerling. Archiv f. Psychiat., 1894, p. 265. Dauber. Deut. Zeitschft. f. Nervheilk., 1893, vol. iv. p. 200. Matthes. Deut. Zeitschft. f. Nervheilk., 1898, vol. xiii.

[6] von Kahlden. Beitrag. z. Path. Anat. und z. allgemein. Path. (Zeigler), vol. xiii. p. 113.

Matthes'[1] case, however, the onset is stated to have been sudden, without previous ill-health, and yet the post-mortem appearances were similar to those of the other recent cases.

A more directly vascular origin for the disease was suggested as early as 1870 by Clifford Allbutt,[2] who considered that a hemorrhage into the cord might explain the symptoms.[3] Allbutt's case, however, of hemorrhage into the cord had but little clinical resemblance to infantile palsy, while it closely resembled the more recently described cases of hæmatomyelia. Hemorrhage in association with myelitis is not uncommon, and small hemorrhages are frequent in infantile palsy, but are there secondary to inflammation.[4] Primary hemorrhage is, however, extremely rare, and is almost invariably due to injury. Pain in the back and paraplegia, including paralysis of the bladder and rectum, are the most prominent symptoms.[5] The hemorrhage does not usually take place into the ventral horns, but more commonly into the dorsal horns, and in cases where a vessel in the ventral horn has given way the blood tends to spread toward the dorsal horn and not upward or downward in the ventral horn. Goldscheider and Flatau,[6] by injecting Berlin blue into the cords of human corpses and of living dogs, found that the ventral horns were specially resistant to such injections, the lines of least resistance for the spread of the injection being along the gray matter of the dorsal horns. Hence it may be said that it has been disproved that primary hemorrhage can be the cause of any cases of infantile paralysis, even those most sudden in their onset.

Embolism need not be considered in the absence of a source for the emboli.

Batten[7] has recently suggested thrombosis of the vessels. After pointing out the peculiarity of the vascular supply of the cord, particularly in the lumbar region, which Moxon showed was derived from very long narrow arteries in which the resistance would obviously be great, and the blood flow therefore sluggish, he shows that the lesions are confined to the distribution of the anterior spinal artery.[8] He further states that thrombosis, whether primary or secondary, does occur in all cases and draws attention to the similarity of the appearances found in the ventral horns of recent cases of infantile paralysis, with the red softening which is seen in the brain after thrombosis of

[1] Matthes. Deut. Zeitschft. f. Nervheilk., 1898, vol. xiii.
[2] Clifford Allbutt. Lancet, 1870, vol. ii. p. 84.
[3] Gowers. Diseases of Nervous System, vol. i. p. 368.
[4] Charlwood Turner. Path. Soc. Trans., 1879, vol. xxx. p. 202. Drummond. Brain, 1885–1886, vol. viii. p. 14. Dauber. Deut. Zeitschft. f. Nervheilk., 1893, p. 200. Chaffey. Path. Soc. Trans., 1886, p. 90.
[5] Batten. Article on Hæmatomyelia. Clifford Allbutt's System of Medicine, vol. vii. p. 44.
[6] Goldscheider and Flatau. Zeitschft. f. klin. Med., 1897, vol. xxx. p. 175.
[7] Batten. Private communication to author and Encyclopedia Medica.
[8] Goldscheider and others. Loc. cit.

the smaller vessels, and that in cases of longer standing the condition is such as would be left after occlusion of the vessels. Thus there is present, according to Batten, a vascular peculiarity in the normal cord, favorable to thrombosis, and appearances such as would be produced by primary thrombosis are found in cases of the disease. He considers that some morbid condition of the blood just precedes the thrombosis, which condition may be due to a number of causes, *e. g.*, recent specific fever, chill, bacterial infection, etc. This theory certainly explains the sudden onset and the vascular distribution of the disease; but it is difficult to understand why thrombosis of these spinal vessels, which is very rare in adults, should be so comparatively common in children, while thrombosis elsewhere is much rarer in children than in adults. The sudden onset of the disease and its vascular distribution is as well explained by supposing that the thrombosis, which probably always occurs to a greater or less extent, is secondary to a local inflammation. Goldscheider,[1] however, in his case of thirteen days' duration, was unable to find definite thrombosis anywhere.

The remarkable special symptoms of infantile paralysis and its occasional occurrence in epidemic form have naturally led observers to search for some specific organism as the cause, but in spite of careful search, Rissler, Goldscheider, Siemerling, Dauber, and others found no organism to account for the disease, and obtained no growth in cultivation experiments. Two recent observers, however, have succeeded in finding organisms in cases of infantile palsy which were similar in appearance to one another and possibly identical. Schultze[2] examined some fluid obtained from the meninges by lumbar puncture in a case which he considered to be infantile paralysis. The pressure of this cerebro-spinal fluid was decidedly increased, but the fluid was clear except for a few specks. In the fluid were found diplococci in chains or tetrads, which were very like the Weichselbaum-Jager meningococcus. No growth was obtained, however, of the organism. Two years after Schultze reported his case, Chapin[3] described a small epidemic, in Poughkeepsie, of anterior poliomyelitis and polyneuritis. In one of the cases, which after death showed the ordinary appearances of anterior poliomyelitis, some diplococci were found by Brooks in the ventral horn of the cord, but none were found in the meninges or blood. In the second case, similar diplococci were found in the blood during life. Here also no growth was obtained. This discovery of the presence of a definite organism in the diseased parts or in the blood is not sufficient for us to accept such organisms as the cause of the complaint. The discovery, however, is important and suggestive,

[1] Goldscheider. Zeitschft. f. klin. Med., 1893, vol. xxiii. p. 509.
[2] Schultze, F. Münch. med. Wochenschrift, 1898, vol. xxxviii. p. 1197.
[3] Chapin. Archives of Pediatrics, November, 1900.

and further researches may find that this organism is constantly present in all cases or in all those of a particular type, and may further show that it can be grown outside the body and its life history studied.

From the evidence at our disposal it is impossible to come to any definite conclusion as to the exact nature of the disease. Clinical records are strongly in favor of at least two, and probably three or four, definite diseases being included under the term anterior poliomyelitis, viz.: 1, that class where the paralysis comes on suddenly without previous ill-health; 2, that class where the onset of the paralysis is preceded by general symptoms, such as fever, vomiting, pain in the back, etc.; 3, the epidemic class, and 4, the adult class. The three latter may possibly be the same disease which may sometimes occur sporadically, and at other times in the form of an epidemic. Occasionally cases occur sporadically which are like the epidemic cases, the disease having spread to the nerve centres in the brain and to the peripheral nerves, and in some of these death even has ensued.

The arguments against regarding hemorrhage into the gray matter of the cord as the cause of any of the cases of infantile paralysis have already been given, and the question of thrombosis has been discussed. In spite, therefore, of the fact that a purely vascular lesion would best explain these striking cases where the onset is absolutely sudden without other sign of ill-health, one is compelled to regard such a cause as improbable. Of the two other possible ways by which the cells in the ventral horns might be destroyed, viz.: a local inflammation or a primary degeneration of the nerve cells, it is impossible at present to quite ignore the latter. An acute degeneration of the nerve cells might be brought about by some poison circulating in the blood, and such a poison might be formed by the growth of the micro-organisms which are the causes of such diseases as scarlet fever, or measles, or by the growth of a micro-organism which is specific to infantile paralysis. Such a primary degeneration of the nerve cells is a possible cause for some cases of infantile paralysis, but the evidence in its favor is very inconclusive. The one definite fact obtainable from the post-mortem examination of patients that have suffered from the disease is that in all recent cases there are signs of a local inflammation in the ventral horns. That these appearances are inflammatory and not due to vascular occlusion is rendered the more probable by the fact that the inflammation sometimes involves other parts than the ventral horns. For instance, Schultze[1] found inflammation of the meninges in an otherwise typical case, and he considered from clinical evidence that the association of meningitis with anterior poliomyelitis was not uncommon. The inflammation, as a rule, however, seems to be confined to the distribu-

[1] Schultze. Münch. med. Wochenschrift., 1898, No. 38, p. 1197.

tion of the anterior spinal artery, and doubtless in the majority of the cases thrombosis occurs very early and so explains the sudden or very rapid loss of power. This local inflammation, like so many inflammations not due to direct injury, is probably caused by a local growth of some micro-organism. No such organism has yet been isolated, and, apart from the observations of Schultze and Chapin, there is no direct evidence of its existence; but the clinical aspects of the disease, as well as the post-mortem appearances, are strongly in favor of this theory. It is possible that the hitherto unisolated organisms that cause measles and scarlet fever might start a local growth, and so a local inflammation in the ventral horn, but the majority of cases of infantile paralysis are not preceded by any acute illness or, indeed, anything that can be regarded as an exciting or predisposing cause. The reputed association with the acute specific fevers would be better explained by supposing that there is a weakened resistance to the attack of other organisms left after these complaints, and such a lessening of resistance would also explain the undoubted frequency with which exposure to chill, damp, or fatigue precedes an attack of acute anterior poliomyelitis in the adult. It is probable, therefore, that the organism associated with anterior poliomyelitis is specific to that disease and is not concerned in the causation of any other morbid condition. Since there seem to be two or more definite diseases included under the name of infantile palsy, there would probably be two or more specific organisms. Beyond this it is at present impossible to go.

REPORT OF A CASE OF ALCOHOLIC MULTIPLE NEURITIS.

By L. W. Atlee, M.D.,
of Philadelphia.

Cases of multiple neuritis due to any one of the several etiological factors are not of infrequent occurrence in the attention of those having special facilities for observation in this class of disease; but to the general practitioner they are so rare as to be seldom or never met with, even in an active practice, and unless he has recently been looking up the subject-matter describing the disease he is likely to be much confused and led into error in his diagnosis when confronted with a case. In a great majority of all cases there are very definite symptoms, but the disease presents a very diverse clinical picture, though certain general features stand out with special prominence.

In the following case the initial rheumatoid pains in the extremities were looked upon by the family physician as due to "rheumatism;" later, the numbness and tingling and slight loss of power in the hands

and feet were viewed as being produced by some obscure spinal disease; and later again, as the disease advanced, the ataxic gait seen in this form of pseudo-tabes led to a diagnosis of true tabes; and at a still later stage of the disease the expansive delirium and motor weakness led a specialist to diagnose the disease as general paralysis.

J. C., aged forty-four years; native of Philadelphia; parents Irish. He is a widower and the father of five healthy children. He is an active working member of a morocco leather firm, and alone was possessed of the secrets of the chemical mixtures used in the process. (His being concerned with chemicals is mentioned, owing to the fact that when he was first seen it was a matter for consideration how much influence lead or arsenic might be having in the production of the disease. This was, of course, prior to having elicited a full history of the case.) When first seen by me, a few days after the specialist had diagnosed general paresis, he was in bed; and as he could give no rational replies to my questions it was, to say the least, most difficult to give to each symptom its proper importance and arrive at a diagnosis. The man was fairly well-nourished looking, the skin moist and greasy; the face was flushed and dilated vessels noticeable over the nose and malar regions. His pulse was 104; temperature in the mouth, 99.5° F. His tongue was heavily coated; the gums soft, spongy, and easily made to bleed. Nothing abnormal could be found in the thoracic organs. The liver was very much enlarged and its edge sharp and hard. His urine showed a heavy deposit of urates and gave a decided haze on boiling and with the contact test. The urea was normal in amount, and there were some hyaline tube-casts in the sediment.

The small muscles of the thumb and fingers were markedly atrophied, as shown by the shrunken appearance of the tissue between the metacarpal bones; the muscles at the back of the forearm concerned in extension of the hand and fingers were also atrophied. These muscles in the palm and forearm were tender on deep pressure, as were also the muscles of the calf and of the sole of the foot. The knee-jerk was absent; the cutaneous reflexes were unaffected. The pupil reflexes were normal; the vesical and rectal sphincters were normal also.

The psychical symptoms were remarkable. He did not at all appreciate his condition, and at times was unconscious of his environment, though he recognized the people about him and could express his wants. When engaged in conversation there was noticeable a sort of silliness —a "childish jocularity"—in what he said. He had delusions of various kinds, at times talking loudly to people he believed to be present, particularly to his wife, who had been dead several years; but most of his delusions were connected with his work at the shop, and he was continually giving orders to the workmen. He did a great deal of travelling in his delirium, and when asked "How are you this morning?" would reply, "Oh, I'm all right to-day—only this soreness in my legs," and then he would branch off suddenly and tell how he had been to Pittsburg or St. Louis to see the "ball game."

He slept very little at night—it was his most delusional and excitable time of the twenty-four hours—but during the day he dozed a good deal. There were two beds in the room, and he frequently moved from one to the other; at times he sat on the edge of the bed, and sometimes he walked through the hall and into the back room. After a good deal

of persuasion he was induced to stand up and to walk. He could do neither with his eyes covered. His gait was very like that of tabes, but his legs were evidently weak from some motor paralysis, though there was no decided "foot-drop." There was nothing remarkable about the man's articulation or manner of speaking, no "scanning," etc.

The history of this case had to be entirely obtained from the relatives, and at first it was impossible to find out how much alcohol had been imbibed as a constant practice all these years; but by dint of interrogating everybody who knew anything about him it became apparent that the patient had been constantly using alcohol for the past eight years at least, although it was an exceedingly exceptional occurrence for him to become what is commonly known as drunk. He never, in fact, missed a day at his work in all this period until his present illness. Some five months ago he began to lose his appetite and to sleep badly; for this he used more spirits, drinking at night when he awoke. At this time he began to complain of numbness and tingling in his hands and feet, and weakness in his legs; and then the feet and hands commenced to swell when they were left in a dependent position for any length of time. Later he had trouble in getting about from the unmanageability of his legs; in other words, the gait became ataxic, as described by those associated with him. The mental condition now was much changed; he became irritable and his memory defective, as shown in forgetting business engagements and the frequency with which he left in the trolley cars a small grip he carried to and from the shop.

In the early stage of the disease the boring pains in the limbs had been regarded as rheumatic and had been treated as such, and when the paretic symptoms became prominent he had been subjected to "electric treatment." This had greatly increased the pains in the limbs, and had been discontinued a few days before he was first seen by me, and also owing to the fact that at the time the disease had been looked upon as general paralysis, and a conformable prognosis given. The electric reaction of the affected muscles was not taken.

After having had the case under observation for a few days and obtained a more candid history of the man's habits, the condition was looked upon as entirely due to multiple neuritis of alcoholic origin, and a more hopeful prognosis given.

The treatment was directed entirely to the correction of the defective general health. All alcohol was withheld, for up to this time he was allowed it in considerable quantities. It was not difficult to do this, owing to the man's mental and physical condition. He was fed frequently with milk and lime-water, strong broths and beef-juice, and gradually his digestion improved sufficiently to take lightly broiled meats and soft-boiled eggs. Mouth-washes corrected the purulent, ulcerating gingivitis and aphthous condition of the buccal mucosa. Bitter tonics, mineral acids, and strychnine were the principal medicinal treatment. When he became very much excited he was given valerianate of ammonia and bromide of sodium. Hyoscine hydrobromate was tried at first, but produced terrible depression, the respiration becoming very shallow and rapid and the heart action weak. For the sleeplessness trional acted excellently and without any apparent after-effect.

At the end of three months' treatment his general health was quite good. All the animal functions were well performed, the muscular power was greatly restored, though the gait was still somewhat ataxic,

and deep pressure into the calf muscles still elicited painful sensations. His mental condition had also changed. When first seen he frequently remained quiet and apathetic for hours, but now he was very irritable and easily excited. At times he perfectly realized his condition and became much depressed, but much of the time he was under the influence of delusions, particularly of persecution—he was being poisoned, he was being bullied and interfered with in the exercise of his will, strange people were being harbored in his house by his relatives; he was continually searching under the bed, in the closets, etc., for these people. At night he was very violent, and as he had now improved so much in general health and muscular power he was difficult to control, and he became personally abusive to those having the constant care of him, so that it was necessary to send him where he could be under surveillance. For this reason he was sent to an institution for the care of the alienated. The following report of his condition after some two months' treatment at this place is very satisfactory: "I am pleased to inform you that J. C. has very much improved in mind of late, and his present condition gives encouragement that he may get well enough to return to his home in the near future. While his mind is comparatively clear, he is still rather delusional; but if he does not suffer a relapse I am in hopes his mind will continue to clear up. His general health is fairly good."

There are few diseases in which an early diagnosis is of greater importance than in multiple neuritis of alcoholic origin. During the *stadium incrementi* prompt treatment would save many patients from months of suffering and disability, since the removal of the cause insures with certainty, during a gradual onset, a quick removal of the symptoms, whereas its effect on the developed disease is manifested much more slowly (Gowers). In forming our diagnosis, if all the symptoms are considered separately for their individual value, and conjointly for their associated significance, it is not often the observer will remain in doubt.

By far the greater number of cases of this disease are slow in their onset unless some other factor is brought into play, as exposure to cold, etc. In the early stages the tingling and numbness in the fingers and toes, palms and soles, and the deep muscular pains, are frequently attributed to "rheumatism." Later, the symmetrical weakness of the extensor muscles of the hand and foot, with hyperæsthesia and deep tenderness, add strength to the diagnosis of multiple neuritis. From the predominance of particular symptoms the disease is divided into a *motor*, *sensory*, and *tabetic* form. The violence of the disease expresses itself particularly in the distribution of the radial and peroneal nerves, which are what is designated as homologous nerves by physiologists.

We must bear in mind that the disease does not often present itself in a classical, stereotyped form; as, for instance, a case may show the feet severely paralyzed and the hands present but sensory symptoms; and although loss of power is the obtrusive feature, some loss of co-ordi-

nation usually accompanies it, and is often the means by which the attention of the patient is first directed to the disability. He finds a difficulty in standing or in performing the finer movements of the fingers; then he may notice for the first time that he has lost power in extending the hand and fingers, or, when walking, to raise the toes from the ground. Whenever there is weakness of the legs the knee-jerk cannot be obtained. "In very rare cases this may persist in a slight degree."[1]

The bladder or rectum are very rarely affected in their innervation in the disturbance caused by polyneuritis. When such symptoms do exist they should suggest involvement of the cord also.

Though the stress of the affection falls on the distribution of the radial and peroneal nerves, the other muscles of the extremities become affected; least and last those about the shoulder and hip. Only in the most extremely severe cases are the muscles of the trunk affected, the diaphragm, and the muscles of the thorax and abdomen; very rarely the facial muscles or those of the tongue; but sometimes the condition of the vocal cords, the rapidity of the pulse, and defective lung circulation suggest affection of the vagus.

Flabbiness and wasting of the muscles are early and marked conditions, and the change in the electric irritability also is early, giving the reaction of degeneration.

The disturbance of sensory nerves is very variable. It is most intense at the ends of the extremities. It usually shows itself in a lessening of the sense of touch and an increase of the sense of pain on stronger pressure. The temperature sense is unchanged.

In the ataxic form (of which alcohol is the most frequent cause) inco-ordination is the chief symptom, and is attributed to affection of the muscle afferent nerves. The inco-ordination so closely resembles that of tabes that it has received the name of *pseudo-tabes* (Gowers), for the pains in the limbs and the loss of the knee-jerk make the resemblance very striking. The ataxia may involve the arms as well as the inferior extremities, but is not nearly so common.

Reflex action from the skin varies much in its condition. In severe cases with much motor and sensory loss it is usually absent.

In prolonged cases we may find trophic changes in the nails, skin, and hairs. These changes are similar to those that occur in ordinary neuritis—glossy skin, arthritic adhesions, and thickening being the most common. Vasomotor disturbances are common, and show themselves in œdema about the ankles, back of the foot, and at the wrist and back of the hand.

The symptoms of multiple neuritis closely resemble those of acute and

[1] Gowers. Diseases of the Nervous System, vol. i. p. 155.

subacute inflammation of the gray matter of the cord—poliomyelitis—but not so much in the alcoholic form as in that due to toxæmias or cold. These symptoms—febrile onset, muscular wasting, and reaction of degeneration, with a tendency to spontaneous recovery, and the initial rheumatic pains—are confusing. In multiple neuritis the localization of the palsy is symmetrical, while in poliomyelitis it is random; in the former we have persistence of the nerve pains, tenderness of the inflamed nerve trunks, and changes in the sensibility—never present in poliomyelitis. The presence of increased myotatic irritability, excessive knee-jerk, and foot clonus would mean disease of the cord.

Pachymeningitis, by damaging the nerve roots, may cause paralysis, wasting, and anæsthesia; but it is rare in this disease to find all four limbs affected. "The legs rarely suffer" (Gowers). The anæsthesia is found in the upper parts of the limbs and the trunk even more than in the distal parts. The nerve trunks are not tender.

In diphtheritic paralysis the disease usually attacks the palate and ciliary muscles first, and there is little if any pain.

The distinction of multiple neuritis from true tabes is often made with great difficulty, especially in that form of neuritis in which the sensory symptoms are predominant and the paralytic symptoms practically absent. It is easy to decide the question when we have distinct loss of power in the extension in addition to the inco-ordination, since there is no actual loss of power in tabes. This should decide the question. In the pseudo-tabetic form of polyneuritis we may have distinct inco-ordination on walking, increased by closure of the eyes, and distinct irregularity in the movements of the feet and legs. These cases perfectly simulate tabes. Pains are common to the two diseases—both acute and prolonged pain and dull rheumatoid—but true "lightning" pains are seldom met with in neuritis. The muscular tenderness is of value as to its being neuritis. In the latter there is no affection of the sphincters, no sense of constriction around the trunk; and lastly, of great importance, the reflex action of the pupil to light is not lost, or so rarely as to be considered so. In neuritis there is no optic-nerve atrophy and no "crises." "Care must be taken not to confound the vomiting of alcoholic gastric disturbance with the gastric crises of tabes" (Gowers). The trophic changes of the two diseases differ The tabetic enlargement of bones and diseases of the joints are unknown in neuritis, while in the latter we have the "glossy skin" and arthritic adhesions, not found in tabes.

In distinguishing multiple neuritis from hysterical palsies the loss of power of extension of the wrist is of great importance, as it is never seen in hysteria.

Multiple neuritis should not give rise to difficulty in its diagnosis from "general paralysis." The peculiar distribution of the motor and sensory symptoms and the loss of the knee-jerk in neuritis are conclu-

sive, the only confusing symptom being the "expansive delirium" sometimes seen in the alcoholic cases.

Severe forms of alcoholic origin when seen late, with damaged kidneys, severe chronic gastric catarrh, and mental torpor, may at first give rise to diagnostic difficulties, as in these cases uræmic symptoms or chronic cerebral meningitis may exist as complications; but time and the bearing of this in mind, and the critical weighing of the history and symptoms, should usually lead to a correct appreciation of the condition.

NOTE.—This man has since returned to his home, and is entirely recovered from all symptoms of this disease.

HEPATIC LESIONS IN INFANCY.

BY MARTHA WOLLSTEIN, M.D.,
PATHOLOGIST TO THE BABIES' HOSPITAL AND TO THE INFANTS' HOSPITAL, RANDALL'S ISLAND.

THE pathology of the liver in infants and young children has not been fully elucidated. A study of 370 consecutive autopsies, made chiefly at the Babies' Hospital, with a few from the Infants' Hospital, on Randall's Island, offers some interesting facts. The ages of the cases studied ranged from two days to four years, but the majority (193) were under six months old; 287 were less than one year of age, and only 31 were over eighteen months. The lesion most frequently encountered was fatty infiltration, which was apparent on gross examination in 214 cases, or 58 per cent., including 45 cases which were tuberculous as well as fatty. Of the remainder, 22 showed tubercles without fatty change, 2 were cirrhotic, 85 deeply congested, and only 47 were normal to the naked eye.

The condition of the infants was noted at the autopsy table as follows: 80, or 22 per cent., were well nourished; 93, or 25 per cent., were fairly nourished; and 197, or 53 per cent., were emaciated.

Fatty Livers. Leaving the 45 tuberculous cases for consideration later, we have 169 simple cases of fatty liver, of which 133 were ordinarily fatty, and 36 extremely so; 80 cases, or 48 per cent., occurred in emaciated infants; 51, or 30 per cent., in fairly well-nourished children, and 38, or 22 per cent., in well-nourished ones. It will be seen, therefore, that the cases of fatty liver occurring in non-tuberculous, emaciated subjects, was 10 per cent. less than the whole number of fatty livers in the autopsy series. Of the extremely fatty livers, 39 per cent. occurred in well-nourished children, and an equal number in emaciated infants; while only 18 per cent. of the ordinarily fatty ones were well nourished, and 50 per cent. were emaciated. So that an extreme degree of fatty infiltration was decidedly more common in

well-nourished subjects, and an ordinary degree of fatty change was somewhat more common in emaciated cases.

Of the extreme cases, 10 were under three months of age, 29 under one year, and 1 over two years. Of the ordinary cases, 26 were less than three months old, 109 were under one year, 19 between one and two years, and 4 over two years.

It is interesting to note the clinical and anatomical diagnosis in these cases. Of *marasmus* there were 97. Considering these in detail, we find that in 22 instances in which no gross anatomical lesion was present at autopsy, the liver was not the seat of fatty change; that in 30 other cases no fatty change had occurred in spite of the presence of pneumonia, 17; enterocolitis, 10; and atelectasis, 3. The pneumonia in these cases was, however, of the hypostatic variety only, and superficial in distribution. The intestinal lesion was merely a mild catarrh, and in no case accompanied by ulceration nor deep-seated infiltration. On the other hand, fatty livers were found in 45 marasmus cases, 46 per cent.; accompanied by bronchitis, 3; malaria and vulvovaginitis, 1; enterocolitis, 14, and bronchopneumonia, 27. These figures bear out Freeman's[1] statement that simple marasmus, unless complicated by an acute disease, is not accompanied by fatty change in the liver.

There were among the whole number of autopsies 67 cases of *tuberculosis*, from two months to three years of age, 29 being under one year and six over two years. Of these, 45 had livers showing both fatty infiltration and tubercles in smaller or larger number; while in 22 no fatty change had occurred. Thus, 67 per cent. of the tuberculous cases were accompanied by fatty liver, while only 55 per cent. of the simple cases showed this lesion. These numbers differ somewhat from Dr. Freeman's; he found that fatty livers do not occur more often with tuberculosis than with other conditions. Among the tuberculous cases were 21 well-nourished infants, of whom 16, or 76 per cent., had fatty livers; 13 fairly nourished children with 8 fatty livers, or 62 per cent.; and 33 emaciated subjects with 20, or 61 per cent. These conditions are directly opposed to those of the simple cases in which the well-nourished infants showed the smallest per cent. of fatty livers, and emaciated infants the highest.

Eleven livers were extremely fatty, 55 per cent. of them occurring in well-nourished cases, and 36 in emaciated ones. Of the ordinarily fatty ones 29 per cent. were well nourished, and 49 per cent. were emaciated. As in the simple cases, the emaciated infants were more prone to fatty change of the ordinary degree, and the well-nourished tuberculous children were rather more liable to extreme fatty infiltration of the liver.

[1] Transactions of the American Pediatric Society, vol. ii., 1899.

Four of the 10 cases of *rhachitis* were accompanied by fatty liver, the cause of death having been bronchopneumonia in 3, and enterocolitis in 1. While in the remaining 6, which were without fatty change, bronchopneumonia was found three times, bronchitis once, enterocolitis once, and enterocolitis with pachymeningitis interna hæmorrhagica once.

In 14 cases of *congenital syphilis* the liver was fatty in 8, all of which were complicated by acute bronchopneumonia, accompanied in 1 case by multiple gummata throughout both lungs. In 1 case, three months old, with erysipelas of the face and pneumonia, the liver was found to be dark-colored and rather soft; it contained a number of small, round, lighter, depressed areas surrounded by a zone of congestion. Microscopically there was intense congestion, with consequent pressure atrophy of many liver cells, and scattered areas of young, cellular connective tissue throughout the organ. Hochsinger[1] says the typical form of syphilitic hepatic disease in infancy is an acute diffuse infiltration with young cellular connective tissue, and that true nodular gummata are rare at this age. No hepatic gummata were encountered in our cases. Only 3 of the 14 cases reached the age of seven, thirteen, and nineteen months, respectively, all the others being under the age of four months—again bearing out Hochsinger's statement that the fatal cases die early. Five of his 16 were less than three months old.

Of 68 cases of *pneumonia*, 45, or 66 per cent., had fatty livers, a decided increase over Freeman's figures; he found only 35 per cent. so affected.

Grouping all the various intestinal lesions under the head of enterocolitis, there were 57 cases with 36 fatty livers, or 63 per cent.

With the acute suppurative inflammation of the serous membranes, fatty infiltration of the liver was very common, occurring in 5 of 7 cases of simple meningitis, 3 of 4 cases of empyema, 2 of 4 cases of peritonitis, and 1 of 2 cases of pericarditis. In 3 cases of pyæmia, and 1 of furunculosis the livers were fatty.

In 2 of 3 cases of measles, all dying of pneumonia, the fatty change occurred. Areas of necrosis were not present. In 1 of the 2 fatal diphtheria cases, 2 cases of influenza, and 2 of malaria (1 dying of acute bronchopneumonia, the other of marasmus) it was also present.

Two cases of sclerema were accompanied by very marked fatty infiltration of the liver.

Thus in the present series fatty livers occurred most often with suppurative inflammations, next in frequency with tuberculosis, pneumonia, and the intestinal diseases. It was never found in uncomplicated marasmus and was inconstant both in syphilis and rhachitis, of which no uncomplicated cases are among our records. Neither disease seemed

[1] Wien. med Wochens., 1892, Bd. 46.

to cause a predisposition to fatty infiltration of the liver. It is to the acute infections that the change in this series of cases must be ascribed.

Cirrhosis. One liver was the seat of hypertrophic cirrhosis. It was the case of a female infant, three months old, with a typical syphilitic eruption, fissured lips, and snuffles. She was fairly well nourished, and entered the hospital for vomiting and diarrhœa. The liver extended 3 cm. below the free border of the ribs, and the spleen was also enlarged. There was no icterus at any time. At the autopsy the liver weighed 205 grammes, was decidedly enlarged, and cut with difficulty, owing to the presence of an increased amount of connective tissue. Microscopically there was a decided increase in the interlobular connective tissue and less of the intralobular. This connective tissue was partly of the cellular, and partly of the older, fibrous variety. The liver cells were granular, and, in places, the seat of pressure atrophy. The gall-ducts were normal in structure and not increased in number. The walls of the small bloodvessels were thickened, the adventitia and the intima being involved. The spleen weighed 150 grammes; it was firm, and the capsule showed chronic perisplenitis. Microscopically hyperplasia was marked.

The only other case of cirrhosis encountered in this series of autopsies was one due to obstruction of the bile-ducts in an infant dying at the age of three months. It is reported elsewhere.[1]

No case of waxy degeneration occurred in these young children.

THE SACROCOCCYGEAL DIMPLES, SINUSES, AND CYSTS.

By Francis H. Markoe, M.D.,
SURGEON TO NEW YORK AND TO ST. LUKE'S HOSPITALS,

AND

Winfield Scott Schley, M.D.,
ASSISTANT SURGEON TO TRINITY HOSPITAL AND TO ST. LUKE'S HOSPITAL OUT-PATIENT DEPARTMENT.

The purpose of this paper is to present a preliminary consideration of the congenital dimples, sinuses, and dermoid cysts found in the median line of the back over the coccyx and lower part of the sacrum, together with a more or less complete review of the literature of the subject to the year 1901.

The presence of these congenital defects occurring in a far larger number of cases than is ordinarily believed has received as yet comparatively little attention from clinicians, having been remarked only

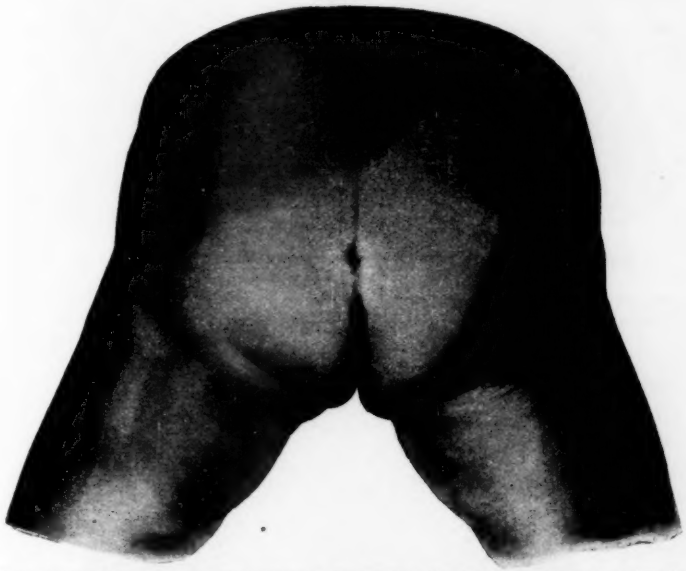
[1] Archives of Pediatrics, March, 1902.

as a rule when some surgical complication, to which the deeper of these structures (the sinuses and cysts) are especially liable, has made a careful examination necessary.

The French authors were the first to regard the differences in development of the sacral region of the trunk, and, therefore, to note those longitudinal furrows or rounded depressions of greater or less depth, found in a large proportion of babies and children and smaller proportion of adults.

A simple examination of adults or children, but especially of babies, by the mere separation of the buttocks, will often show over the coccyx

FIG. 1.



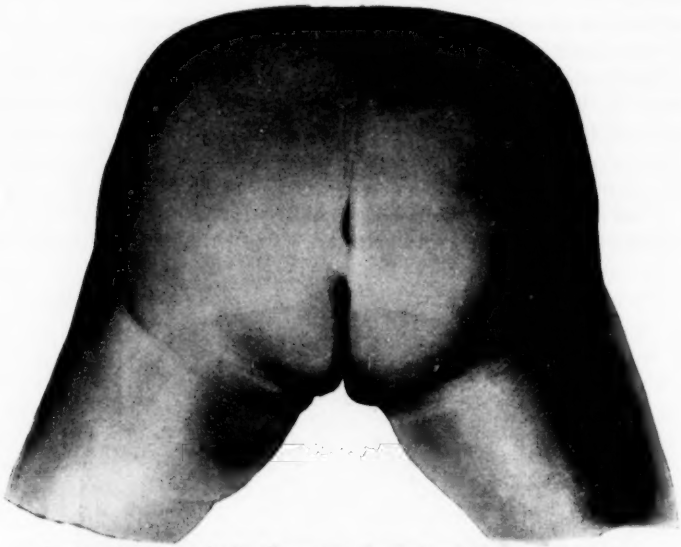
Representing the most common appearance, the shallow dimple. Drawn from ten-days-old baby. Corresponds to A, Fig. 4.

above the anus, some form or degree of dimpling or indentation of the skin, either the longitudinal furrowing or rounded depression, with less frequently a sharply marked deep pit indicating the mouth of a fistula or sinus. (See Figs. 1, 2, and 3.) Nor is it very uncommon to find several members of one family showing the same condition. Such cases have been reported by Madelung and Dunlop.[1]

The integument within and immediately about these little defects usually shows slightly more gloss, is pinker than that over the rest of

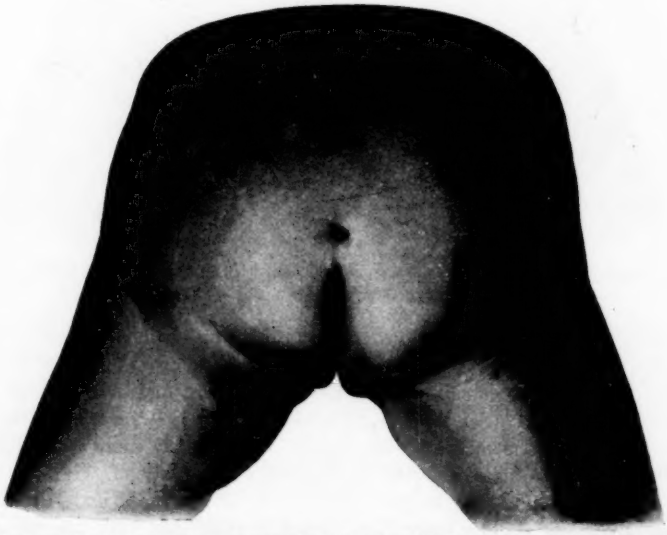
[1] Lancet, London, 1882.

FIG. 2.



Representing the longitudinal furrowing. Drawn from baby about one week old.

FIG. 3.

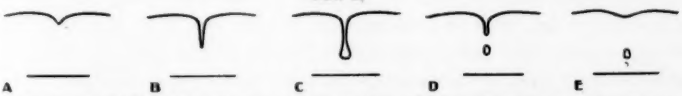


Representing the external appearance of the less frequently found sinus. This may be only a centimetre deep or several centimetres, and may or may not be sacculated at its end. Corresponds to the external appearance of B, C, or D, Fig. 4.

the part, and is moister. From the deeper ones, indeed, clothing in contact with the skin may be decidedly dampened, as instanced in some of the cases of J. M. Warren[1] and others. Pulling upon the skin about these depressions or putting it upon the stretch with the finger demonstrates more than the usual resistance to its gliding on the deeper structures, and at the same time causes an exaggeration of the dimpling, showing an adherence or tacking down to the less movable parts beneath. Hodges,[2] among others, has written of this. It can often be shown where there is but the merest dimpling present, one so slight as to escape ordinary observation. It is to be regarded as quite characteristic of these depressions.

In size and depth they may range from the faintest indentation through sharper and deeper pit-like formations to sinuses of many centimetres depth, possessing the finest orifice or one so large as to be mistaken for the anus itself, as happened in a case reported by Lannelongue.[3] Or we may find over this sacrococcygeal area a completely sequestrated pouch, an epidermoid cyst, with or without outward mani-

FIG. 4.



Diagrammatic sketch of the dimples, sinuses, and cysts in coronal section, and showing the more usual varieties met with. Straight line indicates bone beneath either of sacrum or coccyx; curved line, the skin surface of the buttocks.

festation of the same. Often one or more fistulæ will be found to lead into a cystic formation or sacculated pouching, such as described by Wendelstadt.[4] In fact, "we can demonstrate all possible transitions from the open inversions of the external skin, such as not infrequently occur in the neck in the form of cleft or sinus-like dermoids, to such as have only a very narrow communication with the skin, and finally such as are wholly cut off, as was first demonstrated by Heschl."[5] (See Fig. 4.)

The occurrence of these congenital defects observed in a study of a great number of subjects shows the largest proportion to exist in young babies, and the least in adults. Lannelongue gives 20 to 25 per cent. of all young children. Despres,[6] 30 to 33 per cent. at birth. Heurtaux,[7] 4 to 5 per cent. of adults on a basis of 960 cases examined.

[1] THE AMERICAN JOURNAL OF THE MEDICAL SCIENCES, 1854; Philadelphia Medical Times 1873; Boston Medical and Surgical Journal, 1877, and "Surgical Observations."
[2] Boston Medical and Surgical Journal, 1882.
[3] Bull. Méd., Paris, 1889; Bull. Mém. Soc. de Chir., 1882–1886.
[4] Dissertation, Bonn, 1865.
[5] Präger Vierteljahrsschr., 1860.
[6] Bull. de la Soc. Anat., 1874; Bull. et Mém. Soc. de la Chir., 1889, vol. iv.
[7] Bull. et Mém. Soc. de Chir., 1882.

Lawson Tait,[1] 23 per cent. of women examined at the Birmingham Hospital for Women, which would certainly seem a high percentage for adults. Peyramaure-Duverdier,[2] about 3 per cent. of persons examined. Kulm and Wendelstadt give a somewhat higher percentage. In a series of 300 consecutive births observed in this city, a well-marked dimple or sinus occurred in 100 out of the 300 babies. The series was an absolutely consecutive one, and therefore gives very accurately the true proportion of cases presenting these anomalies.

As regards their situation, it may be noticed anywhere from the anus to well up on the sacrum and always exactly in the middle line. Usually they are situated over the lower part of the coccyx, rarely closer than 1 centimetre to the anus. Mallory[3] gives the situation in order of frequency as:

1. Near tip of coccyx.
2. Sacrococcygeal region.
3. Over lower part of sacrum.
4. Between coccyx and anus.

Nicaise[4] says they occur in three principal places, dorsum of sacrum, sacrococcygeal junction, and tip of coccyx. Lannelongue found in 95 observations that 29 were situated over the sacrum, 38 at the junction of the sacrum and coccyx, and 28 at the tip of the coccyx. Despres believes that they are commoner between the coccyx and the anus, while Lawson Tait believes he has seen the greater number at the upper end of the fold between the nates over the sacrum.

In the series here reported the average distance was 1.66 centimetres above the anus, agreeing more closely with the statistics of Mallory. The nearest to the anus was 1 centimetre, the most distant 3½ centimetres.

There is more often but one dimpling or sinus noted, but occasionally two, more rarely three or more. Lannelongue reports those with three openings. Lamadrid mentions one with three openings, while Heurtaux reports one with three and another case with four congenital openings of sinuses in the middle line of the back. One depression was found ninety-two times, two depressions eight times. Those with three or four were not noted in the above series.

The "depression" of the French, or dimple, or fovea, is by far the most frequent and simplest of the three abnormal formations, *i. e.*, foveæ coccygeæ, fistulæ coccygeæ, and cysticæ coccygeæ.[5]

The sinus is much less frequent. In the 100 cases referred to the foveæ occurred eighty-nine times, while the fistulæ occurred but eleven

[1] Publication, Dublin.
[2] Thèse de Paris, 1882.
[3] The American Journal of the Medical Sciences, 1892.
[4] Tribune Médicale, 1893.
[5] Wette's Classification, Langenbeck's Archiv, 47.

times. Of the relative proportion of the cyst occurrence we can as yet say nothing for lack of sufficient data and histological examination.

By the older writers, before the days of microscopical examination and before any serious attempt at explanation for their occurrence was made, but when the surgical complications of certain of these structures formed subject-matter for literature, they were usually described as "pilous cysts," or "pilonidal sinuses;" or they were styled "furuncles," "abscesses," or "phlegmons," according to the nature of the pathological process occurring and in which they were seen.

The study of these foveæ, fistulæ, and cysticæ is of comparatively recent date, beginning about the year 1868. Courand,[1] reviewing the literature of the subject to the year 1883, declares that he found but fourteen reported cases.

The tumors of this region, on the other hand, were studied many years previously. Meckel and Himly, in 1818, wrote upon fœtal inclusions and parasitic monsters. Ammon, in 1842, Wernher, in 1843, and Velig, at Strassbourg, 1846, Lotzbeck, in 1858, etc., contributed to the literature. One of the first reported cases of sinuses was that of Anderson,[2] in 1847, under the heading, "Hair Extracted from an Ulcer."

Gross,[3] in 1882, speaks of a "congenital pilocystic tumor" sometimes met with upon the coccyx in the vicinity of the anus. "Its origin is apparently connected with a sebaceous follicle, which, during its development, intercepts a small tuft of hair very much as in certain sebaceous formations on the head and face." Vaughan,[4] in 1865, considers their origin involved in obscurity. He reports three cases of "pilous cysts." Lamadrid,[5] 1872, considers them due to imperfect coalescence of the lateral halves of the body. "It is loose hairs which work their way down these preformed sinuses, which cause the irritation and inflammation often observed." J. M. Warren, in his *Surgical Observations*, also considers their origin obscure. Hodges, in 1880, believed as did Lamadrid, that hairs from the surface were the primary source of trouble. Heurtaux, in 1882, believes that epithelial detritus and sebaceous accumulations take place in these congenital infundibula. "This retention can become the cause in certain cases of suppurative inflammation of the skin which forms the bottom of the sinus; the skin becoming ulcerated and perforated, pus gradually infiltrates the subcutaneous tissue and gives rise to the fistulous tract."

What bothered the older observers was the presence of the coil of hair or accumulation which they usually found at the bottom of the sinuses and sacculated dilatations in their suppurative cases. As the

[1] Thèse de Paris, 1883.
[2] Boston Medical and Surgical Journal, 1847.
[3] System of Surgery, vol. ii.
[4] St. Louis Medical and Surgical Journal, 1865.
[5] Philadelphia Medical Times, 1873.

epithelial, sebaceous, and hair-bearing lining was destroyed by the inflammation and often impossible of identification, they had to imagine the strands of hair working down from outside, quite in such a way "as hair-balls are formed in the stomachs of cattle," one writer states. Hodges gives three conditions as essential, "a congenital dimple or sinus, pilous development, and lack of cleanliness."

If no hair was found it was the sebaceous and epithelial accumulation, with little or no means of exit, that caused the trouble. Walker,[1] in 1875, reported a case of "Monstrosity by Inclusion." A sinus over the coccyx was laid open and a coil of light hair found therein. Fere,[2] in 1882, thinks the dimples and sinuses due to incomplete closure of the "posterior umbilicus," *i. e.*, the lower end of the medullary tube. Terrillon,[3] in 1882, considers them due to a special form of spina bifida involving the skin only. Lawson Tait, suggested the "coccygeal dimple" as the "cicatrix of the spina bifida by which the human tail has been lost." Lannelongue, in 1882, believes that "after the medullary canal is formed, the mesoblast passes back between the vertebral column and the external epidermis, except in the region of the sacrum, where little of this tissue is interposed, so that this region is reduced to epidermis and bone. Consequently the superficial layer, the epiblast, joined at a later period to the mesoblast, preserves closer relations with the bone, and at one or more points the skin may be bound down to the bone, and later, when the subcutaneous tissue is developed around these places, a depression will be formed. If deep and narrow enough, the orifice may close up and a dermoid cyst will be the consequence." Wendelstadt, in 1885, expresses the same idea and opinion.

As these congenital dimples and sinuses were not confined in their occurrence to the sacrococcygeal region, but were not infrequently observed in the same localities as the dermoid cysts of regions in which embryonal parts joined, such as the neck, face, roof of the mouth, back of the head, and along the spine, and even in conjunction with these cysts (see the cases of Guzman,[4] Sutton,[5] Stelwagon,[6] Barling,[7] Wagstaffe, etc.), the idea of imperfect closure of the lateral halves of the body or epiblastic involution was usually adduced to explain them. This was the generally accepted explanation up to the time of the article by Tourneux and Herrmann,[8] in 1887, upon the remains of the spinal cord or medullary vestiges in this region.

Tourneux and Herrmann, finding remnants of the spinal cord rudiment behind the coccyx in the fœtus, in a study of this region, believed

[1] Virginia Medical Monthly, 1875.
[2] Bull. de la Soc. Anat., Paris, 1878–1882.
[3] Bull. et Mém. Soc. de Chir., 1882.
[4] Thèse de Paris, 1883.
[5] Journal of Anatomy and Physiology, London, 1886; Annals of Surgery, 1889; Lancet, London, 1889.
[6] Philadelphia Medical Times, 1883.
[7] Annals of Surgery, 1889.
[8] Journ. de Anat. et Phys., Paris, 1887.

them of sufficient importance to account for these structures. Borst[1] gives the salient features of the argument: "At the beginning of the third month the spinal cord reaches to the third last coccygeal vertebra and is continued to the lowest coccygeal vertebra as a bundle of irregularly arranged nerve fibres in which the cells are embedded in groups and rows apparently without distinct regularity, and there is no central lumen. This bundle of fibres is connected with the deep layers of the cutis at the lower end of the spinal column, and these structures form a swelling and a cavity, the latter partly lined with polyhedral epithelium and partly with a form more on the cylindrical order. Owing to the unequal growth of the outer coverings of the spinal column and of the spinal cord, the growth of the soft parts being slower than that of the spinal column, a loop-like formation of this terminal portion of the spinal cord gradually develops, which bends toward the dorsum of the fœtus (horseshoe form of the terminal end).

"The concavity of this loop is directed backward and upward; the two ends of the loop terminate, the one anteriorly and deep seated (descending), and the other posteriorly and superficial (ascending), the latter lying immediately beneath the skin in the deep tissues behind the last coccygeal vertebra. At the end of the third month the conus of the spinal cord is on the level of the junction of the third and fourth sacral vertebra, and below this there is only an epithelial tube surrounded by a thin layer of longitudinal nerve fibres, which structure broadens along the lower coccygeal vertebræ (the descending end) and terminating below in the ascending end as mentioned above; the filum terminale developing out of the upper sacral portion of this cord, while the lower gradually disappears. So the so-called 'ascending' of the spinal cord is not only due to an unequal growth of the spinal cord and spinal column, but also to the fact that a portion of the former undergoes retrograde changes and disappears.

"The deeper end of the before-mentioned loop, as intimated, undergoes retrograde changes by atrophy during the fourth month. But the upper end of the mentioned loop, which at this time lies over the second last coccygeal vertebra under the skin, continues to grow up to the fifth month, then reaching its maximum development ($\frac{2}{3}$ millimetre along the fourth and fifth coccygeal vertebræ); in the formation of strands and heaps of polyhedral cells with irregular cavities lined with cylindrical, cuboid, or polyhedral epithelium, the whole extending from below anteriorly to above posteriorly, and connected with the tip of the coccyx by means of the so-called caudal ligament; this ligament accompanies the entire medullary remnants throughout their whole extent.

[1] Centralblatt. f. Allgem. Path. u. Path. Anat., 1898.

"These mentioned medullary remnants also begin to atrophy after the fifth month; but traces of the same, it is said, can be found in the fully developed newborn.

"At the middle of the sixth month only two or three of the mentioned heaps of cells remain, each possessing a cavity, and in the wall of the latter small, round cavities are found between the cylindrical or flat cells.

"Of the cells lining the central cavities of these structures (Perman[1]) some become flat, resembling squamous epithelium (as that of the superficial skin), which might indicate a return to the former ectodermal type; others become elongated and resemble the cylindrical cell of the ependyma.

"The cells forming the mass of the medullary remnant retain their spherical or polyhedral shape. Ciliated epithelium has not been found in the medullary remnants." These researches introduced a new element in the discussion, and the persistence of these structures was considered by many as productive of sinus and cyst formation in this region.

Sutton, in 1889, considers it more satisfactory to regard these sinuses and cysts as "slight defects in the coalescence of the superficial portions of the medullary folds in the sacrococcygeal region."

Masse,[2] in 1889, agrees substantially with Lannelongue. Mallory, in 1892, working independently of Tourneux and Herrmann, after an examination of the bodies of six fœtuses by section through the sacrum and adjacent tissues, confirms their results. He attributes everything in the way of dermoid structure found over the coccyx and sacrum to these medullary remnants, neural vestiges, or "vestiges coccygiennes" of Tourneux and Herrmann. "These cases show," he says, "that in fœtuses of three to six months there is frequently present over the coccyx a canal lined with epithelium, in some cases connected with the skin, in others not; in some, situated near the skin; in others, near the coccyx. The question naturally arises as to their origin. They may be due either to an extension inward of the epidermis or to the remains of some canal. If due to an extension, or as Lannelongue assumes, to the skin being bound down to the coccyx, why do they not contain the glands and hair follicles with which the epidermis in that region is studded. As regards the extension inward of the skin, why should it occur here so often and nowhere else? It seems much more likely that they are due to incomplete obliteration of a former canal, and extending, as they all do, upward and posteriorly to the coccyx, the medullary canal seems to be the most likely origin.

"The branchial clefts are closed by the eighth week. As before stated, the medullary canal has been open as late as the ninth week,

[1] Langenbeck's Archiv, 1895.
[2] Bull. et Mém. Soc. de Chir., 1889; Bull. gén. de Therap., 1885.

consequently the obliteration of the clefts in the one case, and of the medullary canal in the other, must take place at about the same period of intra-uterine life, with this difference, that the growth is more rapid and perfect in the upper part of the body, and hence more favorable to the closure of the clefts. If, notwithstanding this, sinuses and cysts occur in the neck and about the ears, there is at least an equal chance that they may occur at the lower end of the medullary canal.

"It would seem, from a study of the sections from these fœtuses, that obliteration of the medullary canal takes place at first and most completely at the lower end of the sacrum, and extends from this point in both directions. As is well known, the spinal cord at first extends the whole length of the vertebral canal; but, as the latter grows the more rapidly in length, the cord rises and the filum terminale is stretched, thus favoring obliteration of the medullary canal at the lower part.

"The obliteration of the medullary canal between the end of the vertebral canal and the skin apparently frequently takes place in an irregular manner; but, for that matter, the medullary canal in the spinal cord shows frequent irregularities, sometimes existing as a distinct canal, sometimes double, as in Fœtus VII., and often showing in sections only as a very irregular clump of cells. Undoubtedly, the majority of these remnants of the medullary canal become obliterated; only the larger, especially those in which glands and hairs are present, persisting as the depressions, sinuses, and cysts of extra-uterine life; and in all probability it is only the congenital sinuses and cysts which give rise to the suppurating sinuses."

Nicaise, in a clinical lecture reported in 1893, stated that his belief in the origin of these affairs agreed with that of Lannelongue and the majority of the French and German observers. This idea of epiblastic evolution, he says, was mentioned as far back as 1852 by Verneuil.

Ritschl,[1] in 1892, holds extreme views, believing that not only cysts situated upon the dorsum of the sacrum and coccyx, but cysts lined with stratified squamous epithelium, resembling that of the skin, and situated upon the ventral surface of the coccyx as well, are due to these same medullary remnants of Tourneux, Herrmann, and Mallory.

Aschoff,[2] in 1895, believes that the median agglutination may be the cause of sinuses and dermoid cysts of the dorsum of the sacrum and coccyx. He also says that the caudal extremity of the spinal cord lying on the dorsum curves upward and backward, forming a U-shaped loop, one end of which is connected with the skin. Gradually the loop portion which connects the ends disappears, and at the last the dorsal portion (les vestiges coccygiennes of Tourneux and Herrmann) does the same. The point at which connection with the skin exists, and which

[1] Beitrage zur klin. Chir., 1892. [2] Cysten in Lubarsch's Ostertags Ergib., 1895, vol. ii.

is connected with the coccyx by fibrous strands, is the fovea coccygea. This idea is again referred to by Stolper.[1] Borst, in 1898, is of the opinion that not only the depressions and sinuses, but the cyst formations and many of the more complex tumors of this region are due to these invaginations and agglutinations of the ectoderm. He believes with Lannelongue, Wendelstadt, Aschoff, and others, that the lower portion of the spinal column being the last portion of the posterior opening of the spinal canal to close, that, therefore, the "separation between the external skin and incurved corneal layer of the blastoderm is more difficult, and fibrous agglutinations with the skeleton are more apt to occur." That these fistulæ and depressions are not always connected with the spinal column by the fibrous bands mentioned by Fere and subsequently by Lannelongue (who denies this as an invariable rule), Wendelstadt, Molk,[2] Trendelenburg, and others can be explained upon the basis of their "subsequently becoming looser." He finds that these congenital depressions, sinuses, and cysts of the sacrococcygeal region "show the presence of the external skin in their walls." It is true, he says, as Wette[3] notes, that there are frequent deviations from the normal skin structure, such as thinning of the epithelial covering, absence of the development of papillæ, lack of true corium, poor development, or entire absence of hair, sebaceous and sweat glands; but this is no more than might be expected with such disturbances in development. Furthermore, due to complex conditions of development of this part of the body, these abnormal agglutinations can and often do occur, and "portions of the ectoderm become displaced beneath the surface, and there continue to develop."

Born, he says, having gone over all the work done in this line (Nagel, Mihalkovicz, Keibel, Reichel, Retterer, Tourneux, etc.), states that with the manifold and complicated processes of invagination and agglutination which occur here, epithelial germs can easily become separated and lead to the formation of cysts. Nor is it astonishing that cysts may occur in the perineal region as well, lined either with cylindrical epithelium or epidermis, as the ectodermal plate is able to produce epidermis as well as mucous membrane.

Stolper, in 1899, believes that Mallory and others "go far beyond the indications" in ascribing to the medullary vestiges the formation of these sacrococcygeal defects. "I am of the opinion that for the formation of fistulæ and true dermoid cysts we must also drop the frequently urged theory, or, at least, modify it very much. Particularly in these structures we miss the presence of nerve tissue as a principal constituent." The idea is a less radical one; it is not the medullary vestiges themselves, "but the peculiarities of growth associated with

[1] Deutsche Zeitschrift f. Chir., 1899.
[2] Thèse de Strasbourg, 1868.
[3] Arch. f. klin. Chir., 1894.

their development and atrophy are of interest in the development of fistulæ and cysts." It is the connective-tissue strands accompanying the ascending arm of the U-shaped tube, and which extend from the tip of the coccyx and later form the ligamentum caudale, which "are not without significance in the development of the mentioned depressions and furrows." "Even if the extra-vertebral nerve mass disappears after birth in the physiological way, the easily imagined bilateral continued growth of the accompanying connective-tissue strands may result in the formation of depressions and furrows, which, owing to comparatively early intra-uterine closure of overgrowing epidermis may result in canals. This becomes all the more probable when we consider that the medullary remnants have reached their maximum development at the beginning of the fifth month and begin to atrophy after the sixth month." He believes the epidermoid fistulæ and the sacral dermoid cysts to be a "continued development of the much more frequent and similarly explained foveæ coccygeæ." Both the fistulæ and the cysts are structures of true epidermis and with an epidermoid lining which is continuous with that of the external skin, and both are connected beneath with either the sacrum or the coccyx.

Wette's observations upon the often found relatively incomplete development of the skin lining these structures are also referred to. Owing, however, to the known irregularities in the formation of hair and the hair follicles and sebaceous and sweat glands in the different portions of the external skin, we should not be surprised to find similar irregularities in these complex malformations as seen elsewhere. Two cases are reported in which histological examination of the tissue removed was made. The first case, that of a man, aged thirty-one years, and suffering from an acute inflammation of one of these fistulous tracts (Clinic, Dr. Wagner, Konigschutte) was cured by radical excision of the whole tract. "It was found at several points that the wall of the fistula presented almost exactly the same histological structure as the external skin, except that the layer of epidermis was not so thick and had less of a corneal layer." There were no hair follicles found, but glandular structures very closely resembling sebaceous formations lay deeper in the skin than they are usually found. Disregarding the lesions of the acute inflammatory process and those due to previous curettings, "we had to deal with an open canal, open below, closed above, the wall of which was composed of epidermis throughout." The second case was that of an acute inflammatory process in a congenital sac showing similar conditions. Cure also resulted after radical extirpation. Microscopical examination of the sac here showed a mucous-membrane-like structure without hair follicles and with scant glandular structural development. The tract leading to the dilated portion was lined with granulation tissue, and no direct transition from the skin to

the wall of the fistula could be made out, " but the undisturbed portion showed epidermoid lining."

This last case illustrates the almost completely sequestrated pouch, communicating with the exterior of the body by a narrow fistulous tract only. Some of these invaginations are at the start of considerable size, while others dilate from the closure of their fistulous outlets, the resulting accumulation often augmented by inflammatory products forming a tumor. This class must be grouped with the dermoid cysts.

We have, then, in this sacrococcygeal region three abnormal formations—depressions, sinuses, and cysts—usually communicating with the external surface of the body, sometimes not, and which are lined with a tissue identical with that covering the external surface, namely, skin. Morris[1] has recently reported another case.

That the " vestiges coccygiennes " of Tourneux and Herrmann and Mallory are the remains of the medullary canal there does not seem to be any doubt, and no attempt is made to deny the fact. It is even quite certain that in many cases they form a part of and give rise to the more complex congenital malformations, the tumors of monogerminal origin of this region. But it would certainly seem that here their significance ceases; they are to be regarded merely as a part of the original way of communication between the medullary canal and the skin surface, and are destined for obliteration. Nor have, in all probability, the connective-tissue strands of such importance to Stolper any causative relation with our dimples, sinuses, and cysts. If we are to regard the sinuses and cysts as more advanced forms of the dimple, as is undoubtedly the case, it is difficult to see how the dilated ends of these sinuses, and more particularly the sacculated pouches and the more extensive cyst formations, may be produced by traction of a few strands in this manner. And, too, would these binding strands tend to loosen as age advances, and when we know connective tissue thickens and becomes less mobile? We find, it will be remembered, our largest number of dimples in infancy and childhood.

It would seem that if the medullary remains were earlier or primary forms of our coccygeal defects, we should sometimes find in the latter evidences of the fact in the form of anomalies of the lining skin; the presence of cuboidal, columnar, or intermediate forms of cells approaching the squamous variety of the skin and transitions, one to the other. Likewise, in our medullary vestiges we might expect to find at times irregularities; portions of stratified squamous epithelium or transitional forms with or without persistence of the structure as a whole. Furthermore, as has been mentioned, nerve tissue is notably absent in the walls or in the tissue surrounding our sinuses and dermoid cysts. Histolog-

[1] Annals of Surgery, 1900.

ical examination shows us that in our epidermoid structures nothing but true skin has ever been found, except in those instances where it has not been possible to identify any lining tissue on account of inflammatory changes. As regards "the cells lining the central cavities of these structures (medullary vestiges), some become flat, resembling squamous epithelium (as that of the superficial skin), which might indicate a return to the former ectodermal type. Others become elongated and resemble cylindrical cells of the ependyma. The cells forming the mass of the medullary remnant retain their original spherical or polyhedral shape. Ciliated epithelium has not been found." Mallory mentions columnar and cuboidal epithelium. Tourneux and Herrmann found stratified epithelium of the prismatic type and pavement type. They approach either the cells of the medullary tube or those of the epidermis in their evolution. That the elements of the medullary vestiges, instead of atrophying, may take on a lawless growth, just as occurs in tissue with tumor formation elsewhere in the body, we have reason to believe, as has been said, because tumors of this region have been described containing cysts accompanied by or embedded in nervous or neuroglia tissue. Such are the cases of Gutzeit,[1] Weigert,[2] Wasle,[3] Perman, Schonborn, etc. The cysts in many cases were lined with cuboidal, cylindrical, and stratified squamous epithelium, often one form merging with the other. Such a case was Perman's. "The cysts lined with pavement epithelium not infrequently show the general character of a dermoid cyst; there may be a cornification of the epithelium (Hamel[4]); a development of papillæ (Nasse[5]); hair (Hamel, Lutkemuller,[6] Hildebrand[7]); and of sebaceous and sweat glands (Lutkemuller, Nasse, Hildebrand)."

It is not unusual to find fistulæ and dermoid cysts occurring in conjunction with these complex tumors of this region. Nor is it to be regarded as evidence against their formation from the ectoderm of the surface. Agglutinations and involutions in these cases occurring in similar manner as in uncomplicated cases, while other displacements of ectoderm, or part only of the same, together with medullary remnants and other fœtal structures by proliferation, form the bulk of the tumor mass. (See Schmidt's[8] case.) He found in a three-and-a-half-year-old girl a number of fistulæ in the sacrococcygeal region which communicated with a dermoid containing hair. This was connected to a complex tumor which had a pedicle connection with the spinal column.

Furthermore, we have to consider such cases occurring elsewhere; in the lumbar region or higher (cases of Muscatello,[9] Kaufmann,[10] Wette,

[1] Dissertation, Königsberg, 1896.
[2] Virchow's Archiv, 1875.
[3] Dissertation, Wierzburg, 1896.
[4] Dissertation, München, 1895.
[5] Langenbeck's Archiv, 1893–1895.
[6] Oesterr. med. Jahrb., 1875.
[7] Arch. f. klin. Chir., 1895.
[8] Dissertation, Greifswald, 1889.
[9] Archiv f. klin. Chir., 1894.
[10] Dissertation, Berlin, 1883–1893.

etc.), where there are no medullary vestiges. We find, therefore, except in the large and progressively growing tumor formations on the one hand, medullary remnants, and upon the other, formations of true skin. There are no gradations in these smaller defects. So that it would seem that the epidermal lining of our dimples, sinuses, and cysts was derived from a tissue or cellular structure already differentiated and fixed and subject to no possibility of any other outcome. If this is not so, we will have to believe that the ectoderm of the distal portion of the tube becomes fully developed epidermis, or nothing at all, and disappears. If it is true that we have these dermoid structures, because the surface type of epithelium is developed, then we have a right at times to expect an irregularity in development or an irregular disposition of this epithelium. So far in many cases we have yet to see squamous epithelium of the surface in conjunction with cuboid, spherical, or polyhedral shaped and disposed cells. In the utter lawlessness prevailing in tumor formations in this region, however, this is to be expected, and is found.

Again, we have to consider the cases where two, three, or even four congenital fistulous tracts are seen. It is difficult to see how the ascending end of the vestigial loop can account for these.

The fact that we can demonstrate dimples, sinuses, and cysts along the spinal column, in the neck, face, back of head, and median line, in mouth, etc., where there are no spinal cord remains, but where embryonal parts do meet and fuse, and where involutions or abnormal curvings and agglutinations may occur, seems certainly to establish an analogy in formation with those of the median line in the sacrococcygeal region. Cases of White,[1] Abraham,[2] Sutton, Wagstaffe,[3] etc., are referred to.

Further study of anatomical material upon the embryology of this region will form the basis of a subsequent paper.

Of the dermoid cysts, we speak of the true congenital dermoid lined with squamous epithelium and found usually upon the dorsal surface of the sacrum and coccyx, and which never reaches a size larger than that of the "fist," and "usually does not assume such size until later in life," and even then they are soft and can be "moulded" on pressure (Streit). Sometimes there is a fistulous communication with the skin. Their etiology is that of the depressions and sinuses met with in this region. Stolper considers them together with the dimples and sinuses, which he regards as the simplest forms of abnormality occurring as the result of "disturbance in the approximation of the embryonal component parts at the lower end of the axis skeleton." On the ventral

[1] Transactions of the Pathological Society, London.
[2] Journal of Anatomy and Physiology, London, vol. xv.
[3] Transactions of the Pathological Society, London, 1878.

side of the coccyx and sacrum, sometimes above, but oftener below, the levator ani diaphragm, we also find cystic tumors, "which must be classed as true dermoids." These are usually found of larger size than those of the dorsum. In Deahna's[1] case, pressure ulceration of the vagina and bladder actually happened, the cyst filling the pelvis. In Biernacki's,[2] a similar one prevented childbirth. They seldom, however, reach the size of the teratoid mixed tumors. Sanger[3] believes that this latter class are not truly congenital, but are present "simply as a germinal layer at birth," and must be considered a separate species of tumor. That dermoid cysts of this region are rare is shown by his collection of only eleven cases (three between rectum and coccyx, one between rectum and sacrum, three subperitoneal, in cavity of pelvis under levator ani, three behind rectum in cavity of pelvis, right and left side, one behind and below Douglas' cul-de-sac, but above recto-vaginal septum).

They are not visible as tumors, and are generally met "together with anomalies in the structure and differentiation of the uro-genital apparatus and the anus." They sometimes simulate ovarian or intraligamentary cysts or spina bifida with meningocele. (Death has resulted in two recorded instances from tapping the meningocele cysts mistaken for vaginal cysts and teratoid tumors.) They may rupture after suppuration into the bowel, and their contents—débris, pus, and hair—be passed by rectum. They may be mistaken for periproctitic abscesses. (Collected cases of Sanger, Meyer,[4] von Bergmann, Nasse, etc.)

These dermoid cysts are not confined to the regions immediately in front of and behind the sacrum and coccyx, but are found also in other regions of the pelvic connective tissue. They are noted for their simple construction, Sanger says, and show "no relation to the ovaries, the external skin, and spinal column." He distinguishes those situated high up and those that are low down. The former are more complex structures, generally containing mesodermal and ectodermal tissue, and, therefore, hardly belong to the class of simple, true dermoid cysts, but rather to the teratoid class.

To return to the simple cystic structures of true dermoid character. "The simplest forms of these disturbances, which at the same time tend to throw light on the origin of the larger real dermoid cysts, occur in the form of flat depressions in the skin in the region of the coccyx, or as fistulæ in the same region." Frequently at the end of these fistulæ coccygeæ, lined with epidermis and often containing hair and sweat glands, we find dilatations or cavities, or "a series of epidermoidal sacs (Schmidt[5]) containing atheromatous material, and which may without

[1] Archiv f. Gynäkol., 1876, vol. vii.
[2] Dissertation, Berlin, 1887.
[3] Archiv f. Gynäkol., 1890.
[4] Dissertation, Greifswald, 1896.
[5] Virchow's Archiv, 1888; Arb. aus der Chir. Poliklin. zu Leipzig.

doubt be considered as dermoid cysts formed from the segmented or strangulated ends of such fistulæ;" also these epidermoid fistulæ themselves may, owing to closure of their orifices, dilate and then resemble, and, in fact, constitute, as has been said, dermoid cysts. These cysts may or may not present a dimple or sinus superficially. This character of dermoid is noted for its very slow growth. In this connection the case of Kutz[1] is of interest. He mentions a certain tumor, the size of two fists, situated upon the posterior surface of the sacrum, in a woman, aged fifty-three years, and which was noticeable only as a small nodule at birth. (Cases, also, of Lannelongue, etc.) The simple dermoids of this nature situated upon the ventral surface possess the same character, and may or may not have a dimple or fistulous opening at this site. Usually there is nothing to suggest their presence externally. They are, as a rule, situated between the anterior surfaces of the sacrum and coccyx and the rectum in the loose connective tissue. Birkett's[2] case was probably one of this kind; Sanger[3] classifies it as such, although histological data are scanty. The origin of these cysts is explained upon somewhat different grounds than those given for the structures on the dorsum and probably formed by agglutination of the ectoderm with the skeleton. They stand in very intimate relation "to the cloaca formations and the secondary processes resulting therefrom." Born believes that during and succeeding the cloaca stage, with the processes of invagination and fusions that happen, epithelial germinal cells can become separated and subsequently develop cysts. Aschoff thinks it not astonishing that we find here cysts lined with epidermis or cylindrical epithelium, as the cells of the ectodermal plate are capable of producing epidermis as well as mucous membrane. He instances in this connection the "manifold character" of the urethral mucous membrane which is derived from the urogenital plate. Also, the ectodermal structures concerned in the formation of the cloaca may be used in explanation of the cysts lined with mucous membrane found here. There is, as has been demonstrated (Spee[4]), a "direct transition of entodermal structures into offshoots of the ectoderm" through the normally early obliterated canalis neurentericus, connecting the hind end of the medullary canal and the post-anal intestine. Borst speaks of cysts lined partly with squamous epithelium in this region, which he considers formed from this remnant.

The complex tumors of this ventral region also present cysts lined with stratified, squamous epithelium and mucous membrane and transitional varieties. True dermoid cysts are found forming a part of these complex masses or next to tumors of complex construction. Borst, also, while thoroughly doubting Ritschl's view of the derivation from

[1] Dissertation, München, 1895.
[2] Guy's Hospital Reports, 1859.
[3] Berl. klin. Woch., 1884.
[4] Archiv f. Anat. und Phys., 1889.

the coccygeal vestiges, says that inasmuch as we have sometimes such great disturbances in this region, possibly in stunted conditions of the lower end of the axis skeleton, " portions of the vestiges coccygiennes may be transposed to the ventral side and give rise to tumors."

We find transitions from the simple congenital dermoid cyst to the larger and more complex dermoids, and from these to the simpler mixed or teratoid tumors monogerminal in origin, and from these again to the elaborately complex masses due to a secondary germinal implantation or true fœtal inclusion.

We may regard the foveæ coccygeæ as the simplest of the abnormal disturbances and the mixed teratoid tumors the most complex that occur in this region. All the transition forms are observed. Both Hamel and Masse saw stratified pavement epithelium merge into the ciliated form. Borst and Hildebrand saw cysts that were lined with epithelium resembling that of the intestine, with a basilar border and mucous glands, in which there was a transition to stratified pavement epithelium.

The tumors situated upon the dorsum of the sacrum and coccyx show more or less firm connection with the bone beneath, while those upon the ventral surface have but slight connection, if at all, occasionally being attached to the periosteum. This is what one would expect to find, considering our ideas of origin. That inflammatory changes are prone to occur in the deeper of these structures, the fistulæ, in the pouch-like dilatations often found at their terminations and in the cysts, we have seen. The sebaceous accumulations, proliferated epithelium, and especially hair, products of the lining epidermis, having no outlet, or, at best, a greatly narrowed one, are apt to be retained and lead to irritation and suppurative inflammation. If there be a pre-existing outlet, the pressure of the retained material may re-open it and the result be a persistent chronic or intermittent discharge of pus and débris. If none existed, or the pressure of the accumulation be insufficient to open it, having become sealed through maceration of the skin at the outlet, or if the opening show great disproportion in size, retention and abscess formation result, with the usual consequences: tumor formation with subsequent burrowing of pus and the establishment of secondary fistulous tracts. These fistulous tracts are always to one side of the median line, never in it.

Traumatism of one nature or another is very often the exciting cause for inflammatory change. A blow or nothing more severe than a long period of rest in bed may be sufficient. Wette found seven cases in 15,000 sick persons. He also mentions a case occurring subsequent to the formation of a bed-sore in a typhoid patient. Stolper's first case followed confinement to bed (typhoid). Direct traumatism is, however, more often the exciting cause, as in the case of Routier and

Delens,[1] Goodsall,[2] Anderson,[3] J. M. Warren,[4] etc. Abscess formation followed in periods of time varying from a few weeks to several months or years. The *secondary* sinuses were situated at points close to the median line, well out on the buttock, and from near the sacro-iliac synchondrosis to the upper posterior and inner surface of the thigh on either side. (Goodsall, in the analysis of his cases, thinks the first rupture occurs, usually from one-quarter of an inch to one-half of an inch on the left side of the median line.) Furthermore, these discharging sinuses have frequently been considered to have their origin in a focus of *tubercular disease* occurring in the sacrum or coccyx, with the result that one or the other of these bones has been curetted nearly away. The cases of Beall,[5] Goodsall, Madelung,[6] Gussenbauer[7] and others contain such examples.

The treatment that these cases have usually received has been incision of the abscess formation and curetting of the discharging sinus, followed by the use of carbolic acid or silver nitrate as caustics to destroy the lining membrane or to facilitate healing. The only plan, however, promising complete success is the radical, complete extirpation of the whole tract down to the periosteum of the bones as soon as practicable.

A CASE OF TRANSITORY CYSTINURIA ASSOCIATED WITH DIAMINURIA.

By Milton W. Lewis, M.D.,
and
Charles E. Simon, M.D.,
of Baltimore.

In a previous paper on cystinuria one of us collected all the cases reported up to midsummer, 1899. Including Simon's[8] own case, the number was then 107. Since that time three additional cases have been reported by Warburg,[9] Cammidge and Garrod,[10] and Reid.[11] We

[1] Bull. et Mém. Soc. de Chir., 1888.
[2] St. Bartholomew's Hospital Reports, 1888.
[3] Boston Medical and Surgical Journal, 1847.
[4] The American Journal of the Medical Sciences, 1854; Philadelphia Medical Times, 1873; Boston Medical and Surgical Journal, 1877.
[5] Atlanta Medical and Surgical Journal, 1889.
[6] Centralbl. f. Chir., 1885.
[7] Prag. med. Woch., 1893.
[8] Cystinuria and its Relation to Diaminuria. The American Journal of the Medical Sciences, 1900, vol. cxix.
[9] Ueber Cystinuria. Deut. med. Zeit., 1898; cit. in Centralbl. f. d. med. Wiss., 1899, No. 13, p. 222.
[10] On the Excretion of Diamins in Cystinuria. Journal of Pathology and Bacteriology, 1900, p. 327.
[11] A Case of Cystinuria Ending in Recovery. New York Medical Journal, 1901, vol. lxxiii, No. 16.

have further found the record of a case by Lafleur,[1] which had been previously overlooked, and Dr. Garrod has kindly written us of two other instances observed by himself and Dr. Cammidge, an account of which has not as yet been published. To this number we can add another case, so that the total now reaches 112.

Warburg's case occurred in a young woman, aged twenty-two years, who had suffered a great deal from articular rheumatism from her sixth to her fourteenth year. A short time before her admission to the hospital she had a chill, and complained ever since of lassitude and general malaise. Physical examination showed no abnormality barring some swelling of the cervical and inguinal glands. The urine was cloudy and contained blood and albumin. On microscopical examination large numbers of leucocytes and red blood-corpuscles were found, but casts were absent. Of crystalline elements many crystals of cystin were seen. Two days later high fever again appeared, associated with severe pains in the hip joints. With a gradual improvement in the general condition the amount of cystin diminished and finally disappeared. Two weeks later a similar attack occurred, and with it the cystin reappeared. With a return to the normal the cystinuria ceased. Attacks of colic (renal) had at no time occurred. The urine of the members of the family contained no cystin. An examination for diamins was not made.

The patient of Cammidge and Garrod was a male, aged twenty-two years, who had been admitted to St. Bartholomew's Hospital, London, with a cystin calculus. The urine was examined during two periods of twelve and twenty-nine days, respectively, with an interval of thirty-eight days. On two days only no cystin was seen on simple microscopical examination, but the addition of acetic acid quickly caused a copious precipitation of typical hexagonal plates. Cadaverin was found on two occasions only, though thirty examinations were made in all. Putrescin could not be obtained from the urine, but was apparently present in the feces; and it is interesting to note that on the first day on which diamin was separated from the urine nothing was obtained from the feces, and the only yield from the feces was obtained in the midst of a long period, during which the urine yielded no diamin in spite of careful daily examinations. Leucin and tyrosin were absent, although acicular tufts were obtained with Moreigne's[2] method. But the writers find that what Moreigne regarded as tyrosin was in all likelihood the hydrochlorate of cystin.

Cammidge and Garrod also examined bouillon cultures of various

[1] Proceedings of the Montreal Med. Chir. Society, May 9, 1898; cit. in Philadelphia Medical Journal, 1898, vol. i. p. 910, and reported in the Montreal Med. Journ., by E. M. Eberts, September, 1898.

[2] Arch. de Méd. expér. et d'Anat. pathol., 1899, first series, vol. xi. p. 254.

micro-organisms which had been isolated from their patient's feces, but in no instance were diamins found.

The writers also report that from an alkapton urine no diamins could be obtained by the method of Stadthagen and Brieger,[1] but on benzoylating the urine a crystalline product resulted, which was soluble in alcohol, insoluble in water, and which melted at 196° to 198° C. The nature of this product is unknown. A pure solution of homogentisic acid, however, did not give rise to anything corresponding; but, very curiously, it was obtained from a specimen of urine to which a solution of the acid had been added.

Reid's case occurred in a man, aged thirty-two years, who for over six years had been suffering with painful micturition, and had been treated for gravel and muscular rheumatism by his family physician. Examination of the urethra revealed ulceration, and in the urine cystin was found. Subsequently the cystin apparently disappeared, and Reid regards the favorable outcome as referable to the medicinal treatment which was employed. An examination for diamins, or of the urine of the patient's family for cystin, was not made.

Lafleur's patient was a chlorotic female, twenty-three years old. There was no history of urinary trouble apart from occasional "scalding" during micturition, extending over a period of five months. There was no family history of calculus, and careful examination of the patient's bladder was negative. The urine developed a peculiar faint, greenish-yellow tinge on standing for twenty-four hours, with a distinct odor of hydrogen sulphide. An examination for diamins was not made.

Of the remaining two cases Dr. Garrod writes that in one an examination for diamins could not be made, as the patient declined to co-operate; but in the second what appeared to be pure benzoyl-putrescin was obtained, with a melting-point of 175° to 176° C. The excretion of six days was examined, but the diamin was present only in one specimen.

At this place we also reproduce the brief report of Bödtker's[2] work, which Garrod gives in his paper, as the original is published in Norwegian: During the first two months of the period in which the cystinuria patient was under observation Bödtker succeeded in obtaining from the urine, by the process of Udranszky and Baumann, benzoyl compounds, which were shown by their melting-points and by analysis to be those of putrescin and cadaverin, but the yield was small. Five specimens of feces which were examined yielded no diamins. After the first two months the diamins could no longer be found in the urine,

[1] Berlin. klin. Woch., 1889.

[2] Norsk. Mag. f. Laegevidensk. Christiania, 1892, vol. vii. p. 1220.

although the excretion of cystin continued as long as the patient remained under observation.

The history of our own case, which occurred in the practice of Dr. W. M. Lewis, is as follows:

The patient is a married woman, white, aged forty-six years, and the mother of six children. With the exception of a miscarriage about five years ago, which was followed by tedious convalescence, owing to pelvic inflammatory disease, she had suffered no serious illness up to the time of the present attack. At various times, however, during the past ten or fifteen years she had complained of attacks of "neuralgia" affecting the head and epigastric region, which were occasionally associated with nausea and vomiting. Her husband contracted syphilis early in life, and the children present evidence of the inherited disease. Her family history is bad: Two brothers and a sister died of phthisis; the mother died, at an advanced age, of "asthma;" the father was an alcoholic, and died as the result of injuries which were sustained while intoxicated.

Her present illness began on January 15, 1900, with a sense of oppression about the chest, severe headache, nausea, loss of appetite, pains in the extremities, constipation, and painful and difficult micturition. She was not seen, however, until two weeks later, when the following note was made: The patient is a spare, slightly emaciated woman, of a dark, sallow complexion and anxious countenance. The skin feels moist and clammy. The tongue is covered with a whitish fur. The pulse varies between 80 and 96 per minute, is intermittent, and of low tension. The temperature is 101° F. The respirations are 25, shallow, and attended by a frequent, dry, hacking cough.

Examination of the chest revealed nothing of importance excepting a few scattered râles in the dependent portions of both lungs behind. Abdominal examination also was negative. There was some tenderness about the region of the spleen, but the organ was neither palpable nor its area of dulness increased.

During the following days attacks of severe pain developed in the region of the heart, which extended backward beneath the scapula and down the left arm. These attacks were attended by extreme dyspnœa and associated with a markedly intermittent pulse, which became quite frequent, ranging between 110 and 120. The temperature varied between 101° and 103.4° F. The tongue was dry and covered with a brownish fur. The skin was moist and hot. There was a tendency to delirium. Expectoration was scanty and tenacious. At this time there was dulness on percussion at the left base, associated with distant tubular breathing and a few fine, crackling râles. The respirations numbered 30, and were associated with severe pain in the chest and back. During the attacks of pain about the heart a systolic murmur was also noted, which was audible over the entire præcordia, but heard with maximum intensity at the base. Upon the subsidence of the attacks, which usually lasted from four to six hours, the murmur would disappear, to recur with each following paroxysm. Later in the disease the pulse-rate became much diminished, falling as low as 40 per minute, and it was noted that with the gradual development of the bradycardia the intermittent character of the pulse disappeared. The temperature gradually reached the normal, the area of dulness at the left base disappeared,

the pulse-rate returned to normal, and by April 10th no symptoms of the recorded illness remained.

A specimen of urine voided on the day of the first examination was highly colored, strongly acid in reaction, and of a specific gravity of 1.025. Albumin was present in considerable amount; the uric acid was much increased; the amount of indican was apparently below normal; sugar was absent. On standing, an abundant, granular-looking, and glistening white sediment collected, which contained a few red corpuscles, leucocytes, and epithelial cells from the genitalia. Casts were then not found. The most interesting feature was the presence of large numbers of colorless hexagonal plates, occurring both singly and in groups, which were soluble in hydrochloric acid and ammonia and insoluble in acetic acid, and which were accordingly regarded as cystin. The amount was not estimated, but was considerable. Daily examinations of the urine were then made for about one month, and it was noted that during the first four or five days crystals of cystin were uniformly present, but never again in such large numbers as on the first day. After the fifth day, very curiously, the substance could no longer be demonstrated either in the sediment of the native urine or after the addition of acetic acid (two years have now elapsed), and to the present day it has not reappeared. Previous to the disease cystin had never been seen in the woman's urine, although Dr. Lewis had made microscopical examinations on several occasions. Attempts on four successive days to isolate diamins from the collected urine of twenty-four hours led to no definite result. On benzoylating the urine according to Baumann's method a small amount of a gummy, brownish substance was obtained, which was soluble in alcohol and insoluble in water. The material was lost, however, during subsequent attempts at crystallization.

As it was thus likely that diamins, if present at all, were to be found only in traces, it was decided to collect the urine in bulk and to examine large amounts at one time; 12,000 c.c. in all were obtained and benzoylated as usual. After separation from the phosphates the alcoholic solution was concentrated to a small volume and poured into thirty times its volume of water. The precipitate which was thus obtained consisted of the same brown, gummy material as before, but in correspondingly larger amount. The solution in alcohol and precipitation with water was repeated twice, but even then no crystals could be obtained. Thinking that the presence of so much of the brown pigment prevented crystallization, the gummy material was again dissolved in alcohol and the solution filtered through animal charcoal. In this manner the greater portion of the pigment was removed, but at the same time a not inconsiderable fraction of the benzoylated material was lost. Efforts to recover this were abandoned, owing to the difficulty of separating the benzoylated material from the pigment. The alcoholic filtrate was now concentrated to a very small volume and then filtered directly into the water while the latter was actively stirred. A tendency on the part of the benzoylated substance to separate out as gummy material was then still observed, but was effectually combated by allowing the alcoholic solution to flow into the water, drop by drop, and stirring all the time. In this manner a milky looking fluid was finally obtained from which no gummy material whatever separated out. On standing for about thirty minutes a grayish, granular-looking sediment began to form, which on microscopical examination was seen

to be composed of delicate, almost colorless platelets and fine, acicular crystals. The total amount of substance which was thus obtained weighed 0.3827 gramme. The crystals were readily soluble in alcohol, insoluble in water, and very sparingly soluble in ether; their melting-point was 129° C., corresponding to that of cadaverin. Putrescin was not found.

Tyrosin could not be demonstrated in the urine according to common methods; but, like Garrod, we were able to show that from pure cystin, when treated according to Moreigne's method, fine crystals of the hydrochlorate can be obtained, which on microscopical examination alone might be mistaken for tyrosin.

A single examination of the feces for diamins led to no result.

The urine of the patient's children and of a brother contained no cystin, nor could a sulphur reaction be obtained.

Our case of cystinuria is thus the seventh in which diamins could be demonstrated in the urine.[1] Both cadaverin and putrescin together have thus far only been found by Baumann and Udranszky and Bödtker; cadaverin alone by Stadthagen and Brieger, by Cammidge and Garrod, by Simon, and in the present instances, and putrescin only by Cammidge and Garrod in their second case.

From the feces of Baumann and Udranszky's patient both diamins were obtained. Putrescin was found by Cammidge and Garrod in one of their cases, and cadaverin by Simon in his first case. In the remaining cases the results were negative.

In his first paper Simon suggested that in future cases of cystinuria repeated examinations should be made before drawing conclusions as to the absence of diamins, and that amorphous precipitates, which may be obtained on pouring the alcoholic solution of the benzoylated products into water, should be purified with special care, so as to favor crystallization of any benzoylated diamins that might be present. Experience has since shown that, as a matter of fact, diamins may be apparently absent from the urine for days, weeks, and possibly months, even though the cystinuria continues; or if not absent, then present in so small amounts as to escape detection with the available methods if the urine of only twenty-fours hours is examined. In the present case we obtained no definite result on four occasions on which twenty-four-hour lots were examined, while we were successful with larger quantities. It might, of course, be argued that in our case the diamins were present on one or two occasions only while the urine of a number of days was collected, and absent on others. But of this we are not convinced. We believe

[1] The first case was that of Udranszky and Baumann (Zeitschr. f. physiol. Chem., 1889, vol. xiii. p. 562; see also Garcia, ibid., 1893, vol. xvii. p. 577, and Pfeiffer, who quotes a further examination of this case by Baumann, Centralbl. f. d. Krankh. d. Harn. u. Sex. Organe, 1897, vol. viii. p. 173). The second and third cases are those of Stadthagen and Brieger (Berlin. klin. Woch., 1889, vol. xxvi. p. 344). The third is the case of Bödtker (loc. cit.); the fourth is Simon's first case (loc. cit.); and the fifth and sixth are those of Cammidge and Garrod (loc. cit. and above).

that they were uniformly present, though in small amounts, and are prompted in our supposition by the fact that even during the first four days a small amount of benzoylated material was obtained, which was soluble in alcohol and insoluble in water. This was lost during repeated attempts at purification by solution in alcohol and reprecipitation with water. But it will be recalled that later, when working with larger amounts, we obtained this same material apparently, but succeeded in bringing it to crystallization.

But while we believe that every case of cystinuria is associated with diaminuria, we have convinced ourselves that the diaminuria does not necessarily coincide in point of time with the cystinuria, and that, like the cystinuria, the diminuria also may be a temporary event.

Temporary cystinuria appears to be more common than was once supposed, and renders the condition even more interesting. In our case the elimination of cystin apparently only existed during a number of days, and appeared to be in some manner connected with the patient's illness. In Ebstein's[1] case the condition persisted for about ten days and then disappeared.

In Smith's[2] two cases the cystin crystals were only found on one occasion, and Reid reports that in his case also the cystin disappeared and remained absent even after a year had elapsed from the time of the first observation. But we cannot regard this disappearance as evidence of a cure brought about by the administration of medicines, as Reid supposes.

As regards the origin of cystinuria, we still maintain the views expressed in a previous paper, viz., that the condition is essentially referable to a metabolic anomaly and not due to a specific microbic infection of the digestive tract. We may further add that our supposition concerning the relation existing between cadaverin and lysin on the one hand, and between putrescin and ornithin on the other, has since been firmly established. Our own investigations in this direction could, unfortunately, not be continued for reasons which lay beyond our control; but Ellinger[3] has shown that through the activity of micro-organisms, at any rate, the transformation of ornithin to putrescin, and of lysin to cadaverin can actually be effected.

It has further been shown by Mörner[4] and Embden[5] that on hydrolytic decomposition of keratin considerable amounts of cystin can always be obtained, and that of the true albumins egg albumin, serum albumin, and edestin, at least, yield cysteïn under similar conditions. It

[1] Deutsch. Arch. f. klin. Med., 1879, vol. xxiii. p. 138.
[2] Practitioner, 1898, vol. i. p. 475.
[3] Zeitsch. f. physiol. Chem., 1900, vol. xxix. p. 334.
[4] Cystin ein Spaltungsprodukt d. Hornsubstanz. Ibid., 1899, vol. xxviii. p. 595.
[5] Ueber d. Nachweis v. Cystin u. Cysteïn unter d. Spaltungsprodukten d. Eiweissköper Ibid., 1901, vol. xxxii. p. 94.

accordingly appears that in addition to various other groups the albuminous molecule also contains a cysteïn group or even one of its dithio-compounds. In such an event it would not be necessary to imagine a substitution of an HS group for a hydrogen atom of phenyl-alanin, which we previously suggested as the mother substance of cysteïn; but we may suppose that the entire group is split off directly, and then escapes oxidation, owing to the activity of some factor of which we are as yet in ignorance, but which probably represents the direct cause of the cystinuria. The diamins, of course, suggest themselves in this connection; but it is to be noted that Baumann and Udranszky[1] failed to produce cystinuria in dogs by the administration of diamins. On the other hand, it might be argued that under normal conditions the diamins would be immediately destroyed, and that in cystinuric individuals a certain insufficiency may exist which prevents their destruction. Of the actual existence of such an insufficiency we believe there can be but little doubt, but we are nevertheless scarcely prepared to admit that a causative relation exists between the cystinuria and the diaminuria, and we still believe that both are the outcome of a third factor which is still unknown. Whether or not any one of the tissue ferments may here be of moment future researches will show.

THE CAUSES AND VARIETIES OF CHRONIC INTERSTITIAL PANCREATITIS.

By Eugene L. Opie, M.D.,
ASSOCIATE IN PATHOLOGY IN THE JOHNS HOPKINS UNIVERSITY.
(From the Pathological Laboratory of the Johns Hopkins University and Hospital.)

Little systematic study has been devoted to the varieties and to the causes of chronic inflammation of the pancreas. Since the lesion is relatively uncommon, and, though affecting an organ having functions of great importance, is rarely associated with symptoms by which it can be recognized during life, it has, as might be expected, failed to attract the attention given to corresponding alterations of the liver and kidneys. The causal relationship of pancreatic disease to diabetes mellitus and to disseminated fat necrosis now recognized, has emphasized the importance of lesions of the organ.

Changes in the gland, notably chronic inflammation, are seldom primary, but are associated with and usually the result of changes in other organs, the adjacent part of the gastro-intestinal tract, the liver and the bile passages. Inflammatory irritants may reach the gland by

[1] Weitere Beiträge z. Kenntniss d. Cystinurie. Ibid., 1891, vol. xv. p. 77.

the ducts, by the lymphatics, and by the bloodvessels. Obstruction of the pancreatic duct is followed by chronic inflammatory changes, retention of the secretion being associated with alterations of the gland cells and proliferation of the connective-tissue stroma. Opening upon the mucous membrane of the duodenum in company with the common bile duct, the pancreatic duct is exposed to the invasion of bacteria from the intestines and from the inflamed biliary passages. Changes in the bloodvessels, arterial sclerosis, and venous stasis by altering the nutrition of the parenchyma are believed to cause chronic inflammation, while a more important factor in its production is the action of various toxic substances brought by the blood, syphilis, tuberculosis, and alcoholic excesses being assigned as causes.

Carnot,[1] who produced chronic pancreatitis experimentally by a variety of means, designates the condition as (*a*) mechanical, produced by obstruction of the duct, and as (*b*) toxic or (*c*) infectious, caused by the action of toxic substances or of bacteria carried to the gland by the blood or by the lymph or by way of the duct. As he points out, such a classification cannot be applied to the varieties of chronic pancreatic inflammation observed in human cases after death, since in many instances the etiological factors concerned are no longer demonstrable.

From the clinical records of the Johns Hopkins Hospital and the autopsy protocols of the pathological laboratory of the University and Hospital twenty-nine cases of chronic interstitial pancreatitis are available, and in all of these cases material has been preserved for microscopical examination. In the present study the attempt has been made to determine the factors concerned in the production of the lesion, as well as its character. Of twenty-nine cases seventeen occurred in males and twelve in females. The following table indicates the age of the individuals in whom the lesion was observed:

10	to	20 years	1	case.
20	"	30 "	2	cases.
30	"	40 "	2	"
40	"	50 "	9	"
50	"	60 "	11	"
60	"	70 "	2	"
70	"	80 "	2	"

Over two-thirds of the cases occurred between the ages of forty and sixty years.

In ten of the cases chronic inflammation followed partial or complete obstruction of the pancreatic ducts. In one case complete occlusion of the portal vein was accompanied by moderate proliferation of the inter-

[1] Thesis, Paris, 1898.

stitial tissue; in one case the lesion was associated with a condition of wide-spread pigmentation, described by von Recklinghausen under the name hæmochromatosis. In the remaining seventeen cases the etiology of the condition was somewhat more obscure, but is in most of them discoverable. In a preceding report[1] I have described the histology of chronic interstitial pancreatitis and attempted to distinguish the anatomical varieties which occur. Two types of chronic inflammation are distinguishable: (*a*) interlobular, where the newly-formed connective tissue is in great part between the lobules, invading them only secondarily and implicating the islands of Langerhans only when the sclerotic process has reached a very advanced grade; (*b*) interacinar, when the process is diffuse, invading the lobules, separating individual acini, and implicating the islands of Langerhans.

When the interlobular tissue is chiefly affected, the pancreas is densely hard in consistence and has a nodular or granular surface; on section the normal loose aveolar tissue uniting the lobules is replaced by dense sclerotic bands, so that the gland is more compact in structure, the lobules being firmly held together. When the interacinar tissue is chiefly affected the lesion may not be recognized macroscopically; the gland is firmer than usual, but is tough rather than hard. With both varieties of inflammation the stroma may be abundantly infiltrated with fat, which may contain small foci of necrosis.

In the present study, based upon a much larger number of cases (including those formerly studied), I have found the two types named. In twenty-one cases the lesion was interlobular, in eight interacinar. The attempt will be made to determine not only the etiology of the inflammatory change, but the variety of the lesion associated with a given etiological factor.

Obstruction of the Pancreatic Ducts. The usual causes of duct obstruction are calculi within the duct of Wirsung or in the adjacent terminal part of the common bile duct and carcinoma compressing or invading the pancreas. Ligation of the ducts in animals is followed by sclerosis of the gland. Arnozan and Vaillard[2] have studied the progress of the lesion in rabbits, and advance the suggestion that it is caused by the ferment present in the retained secretions. Carnot thinks that a variety of factors are active in its production. The retained secretion, he thinks, has a toxic action upon the glandular cells, while the presence of bacteria invading from the duodenum the pent-up secretion has an important influence on the changes which follow. Reflex nervous stimuli are no longer capable of exciting normal unctional activity, and, he suggests, no longer exert an influence on the

[1] Journal of Experimental Medicine, 1901, vol. v. p. 397.
[2] Arch. de Phys. norm. et path., 1884, 3 s. vol. iii. p. 287.

secreting cells, which, like voluntary muscle cells after section of their motor nerve, atrophy. One or more of these conditions are doubtless always present, but their relative importance is difficult to determine. In many of the cases to be described evidence of infection was present, and it is often impossible to determine how far it was responsible for the lesion.

The pancreas is usually provided with two anastomosing ducts, of which the lower opening with the common bile duct into the duodenum is the larger. Occasionally the upper duct or duct of Santorini is the larger and its orifice is widely patent, but in the majority of cases the smaller duct is functionally a branch of the larger and its duodenal orifice, which is usually patent, is too minute to act as an outlet for the entire pancreatic secretion.

Pancreatic Calculi. In two cases which have been previously reported[1] with greater detail, advanced chronic inflammation was referable to the presence of numerous calculi in the pancreatic ducts.

Case I.—W. H., male, aged forty-three years, had used alcohol (beer) in large quantity. His father died with tuberculosis. Ten months before his death he had had an attack of jaundice.

Clinical Diagnosis. Pulmonary tuberculosis.

Anatomical Diagnosis. Chronic pulmonary tuberculosis; cirrhosis of the liver; pancreatic calculi; chronic interlobular pancreatitis, with fat infiltration; parapancreatic fat necrosis.

Case II.—H. R., male, aged fifty years, states that he has been accustomed to drink whiskey in large quantity.

Clinical Diagnosis. Diabetes mellitus; pulmonary tuberculosis.

Anatomical Diagnosis. Pancreatic calculi; chronic pancreatitis; chronic pulmonary tuberculosis; chronic diffuse nephritis.

In both cases dense sclerotic tissue, in one instance containing fat in large quantity, had in great part replaced the parenchyma of the gland. The islands of Langerhans had, in part, resisted the sclerotic process and had undergone disintegration only when, as in Case II., they were wholly isolated in dense bands of scar-like fibrous tissue. When small patches of parenchyma consisting of small groups of lobules persist, the tissue is remarkably well preserved, and there is little if any thickening of the stroma between the acini. Diabetes mellitus present in Case II. was of mild type and disappeared when the patient was put upon a diet poor in carbohydrates.

Biliary Calculi. The relationship of chronic inflammation of the pancreas to cholelithiasis has excited much interest since Riedel[2] directed attention to the induration of the head of the gland at times observed during operations undertaken for the removal of gallstones, and readily mistaken for malignant growth. In three of one hundred and twenty-two such operations he noticed this condition and suspected the pres-

[1] Loc. cit.

[2] Berliner klin. Wochenschr., 1896, vol. xxx. pp. 1, 32.

ence of carcinoma, but the subsequent history disproved this supposition, and an autopsy obtained in one case demonstrated the presence of chronic inflammation of the gland. Mayo Robson[1] has described two cases in which at operation for gallstones in the common bile duct the head of the pancreas was found so indurated that a diagnosis of malignant growth was made. In one of these cases autopsy demonstrated the existence of chronic interstitial pancreatitis, and since in the second case the subsequent history disproved the diagnosis of carcinoma, Robson thinks that here also chronic pancreatitis was present.

The following cases give additional evidence of the association of chronic inflammation of the pancreas and cholelithiasis, and demonstrate a mechanism by which this change is produced.

Case III.—The patient, male, aged sixty-three years, states that he has drunk whiskey in considerable quantity, but otherwise his personal history is unimportant. Two years and four months before his death he had an attack of jaundice lasting five months. A year later he was admitted to the service of Dr. Halsted with jaundice, associated with repeated chills, and an operation was performed, but owing to the density of the adhesions present it was found impossible to explore the bile passages. After the operation his condition improved, and he was fairly well until two and a half months before his death, when he was admitted to the service of Dr. Osler with jaundice and ascites; the liver dulness was decreased in extent. The abdomen was tapped three times and on each occasion about eight litres of fluid were withdrawn. The patient died with symptoms of a general infection, and a culture made from the blood before death demonstrated the presence of Streptococcus pyogenes. The urine at no time contained sugar. The autopsy was performed by Dr. W. G. MacCallum.

Anatomical Diagnosis. Cholelithiasis; contraction of the gall-bladder; calculus in the common bile-duct; dilatation of bile-ducts; cirrhosis of the liver; chronic interlobular pancreatitis; serofibrinous peritonitis; chronic nephritis; arterial sclerosis; diverticula of duodenum.

The common bile duct is greatly dilated and enters the duodenum beside a small diverticulum of the intestinal mucosa. Near its termination, but just above its junction with the duct of Wirsung, is a large oval gallstone (1.5 x 0.8 x 0.8 cm.) firmly wedged into the common duct in such a position as to compress the terminal part of the pancreatic duct which, as it enters the diverticulum of Vater, passes immediately below the stone. The pancreas is firm in consistence and compact in texture. The duct of Santorini joins the duct of Wirsung, of which it appears to be a branch, and approaches the wall of the duodenum, terminating in a minute papilla which is not demonstrably patent. The liver has a rough granular surface and is tough in consistence.

Microscopical examination of the pancreas shows that the loose interlobular areolar tissue is replaced by bands of dense sclerotic tissue containing many collections of lymphoid cells with a smaller number of plasma cells and polynuclear leucocytes. Within the lobules there is relatively little increase of the interstitial tissue.

[1] Lancet, 1900, vol. ii. p. 235.

A small calculus I have shown in a previous report[1] may lodge at the orifice of the diverticulum of Vater and occluding it may convert the common bile duct and the duct of Wirsung into a continuous channel, thus causing the penetration of bile into the pancreas and consequent acute hemorrhagic pancreatitis. A larger calculus present in the diverticulum of Vater, or in the common bile duct, or slightly above its point of junction with the pancreatic duct, may temporarily or permanently occlude the latter and produce chronic inflammatory changes resembling those which follow ligation of the duct in animals. Doubtless bacterial infection often plays a part in the production of the lesion, and in the two following cases the bile passages containing gallstones are the seat of an acute suppurative inflammation which has been propagated along the duct of Wirsung.

CASE IV.—Female, aged fifty years.

Anatomical Diagnosis. Cholelithiasis; calculi in gall-bladder, cystic, hepatic, and common bile ducts; adenocarcinoma of gall-bladder; metastases in liver; jaundice; suppurative cholangitis; chronic interlobular pancreatitis; peripancreatic fat necrosis.

The liver is deeply jaundiced and is the seat of numerous small abscesses. The gall-bladder, whose wall is thickened by a carcinomatous growth, is contracted over a number of faceted gallstones. The hepatic, cystic, and common bile-ducts near their point of junction are dilated and contain two faceted calculi. The remainder of the common duct is not markedly dilated, but the walls are somewhat thickened and fibrous. The pancreas is very firm in consistence and is infiltrated with fat containing small opaque white foci of necrosis.

Microscopical examination of the liver shows numerous foci of necrosis and suppuration. The normal lobulation of the pancreas is much accentuated by a marked increase of the interlobular tissue. The medium-sized ducts are moderately dilated and contain polynuclear leucocytes in small number.

CASE V.—The patient, female, aged seventy years, was admitted to the service of Dr. Osler, complaining of swelling of the abdomen and legs. Her present illness began eight months before her death, and since this time she has had chills every second or third day. The abdomen and legs have been swollen for two months. She has not been jaundiced and there has been no nausea or vomiting. The bowels have moved not more than once a week. On admission to the hospital, a month before her death, she was emaciated and general anasarca was present. The leucocytes numbered from 33,000 to 27,000. For three weeks before her death the temperature was continuously subnormal. The urine contained numerous casts and albumin in abundance, but no sugar.

Anatomical Diagnosis. Cholelithiasis; suppurative cholangitis; cirrhosis of the liver; chronic interlobular pancreatitis; chronic diffuse nephritis; amyloid kidneys; brown atrophy of the heart.

The gall-bladder, adherent to adjacent organs, contains pale, turbid bile and two faceted calculi. The common bile duct is patent. The

[1] Johns Hopkins Hospital Bulletin, 1901, vol. xii. p. 182.

liver, of which the interstitial tissue is increased, contains small abscesses. The pancreas is large and very firm, and in the adjacent fat are minute spots of fat necrosis. Its ducts are dilated and contain viscid material. Microscopical examination of the pancreas shows a marked proliferation of the interlobular tissue, which is dense and fibrous, but rich in lymphoid cells. The duct of Wirsung and its branches are dilated and contain polynuclear leucocytes and red blood-corpuscles, while their walls are infiltrated with polynuclear leucocytes. The interstitial tissue of the liver, much increased about the portal spaces, is dense and sclerotic and contains polynuclear leucocytes. The small ducts are often greatly distended and filled with polynuclear leucocytes.

In Case III. a calculus in the common bile-duct occupied a position in which it compressed the pancreatic duct; the lesser pancreatic duct was not demonstrably patent. Chronic interlobular pancreatitis was the result of duct obstruction, with perhaps secondary invasion of bacteria. In Cases IV. and V. no calculus was found compressing the pancreatic duct, but in Case IV. one may have occupied such a position at some previous time. In Case V. the history gives no evidence of the passage of a calculus along the duct, and chronic inflammatory changes in the pancreas are presumably the result of an ascending infection originating in the acutely inflamed bile passages. In support of this conclusion there exists an acute inflammation of the pancreatic ducts.

Malignant Growth. In five cases chronic interstitial pancreatitis was caused by a malignant growth compressing or invading the organ. In the following case, which may serve as an illustration of this condition, a primary carcinoma of the pancreas arising in the head of the gland compressed the duct of Wirsung and produced chronic interstitial inflammation accompanied by the formation of cysts.

Case VI.—The patient, female, aged forty-one years, became jaundiced nine months before her death. She gives no history of having had syphilis. A tumor mass was palpable in the umbilical region. The autopsy was performed by Dr. Flexner.

Anatomical Diagnosis. Adenocarcinoma of the pancreas; compression of the bile and pancreatic ducts; jaundice; chronic interlobular pancreatitis; metastatic carcinoma of the retroperitoneal lymph glands.

The tumor, which arises from the pancreas, consists of two masses, between which the remains of the head and part of the body lie compressed. A fibrous capsule separates the tumor from the gland parenchyma. Numerous cysts about the size of a walnut occupy the body and tail, and are present, but less numerous, in the duodenal end. A probe can be passed along the compressed duct.

Microscopical examination shows throughout the gland a moderate increase of the interstitial tissue between the lobules and in less degree within them. Cysts lined by a single layer of cubical or flat epithelium are abundant in the body and tail.

In the second case (Case VII. of the present series) previously described,[1] advanced chronic interstitial inflammation followed the development of a carcinoma of the bile papilla and diverticulum of Vater. The carcinomatous tissue was removed at operation, and the biliary and pancreatic ducts were transplanted into the duodenum. At autopsy the duodenum was the seat of an extensive carcinomatous ulcer, into the base of which the pancreatic duct opened. Marked dilatation of the pancreatic duct gave evidence of its partial obstruction. Infection from the ulcerated surface upon which the duct opened was with great probability an important factor in producing the advanced chronic interstitial inflammation which resulted.

In three cases (Cases VIII., IX., and X.) chronic inflammatory changes were associated with the invasion of the gland by a carcinomatous new-growth of the stomach. When the head of the gland is invaded there is a diffuse interstitial change; but where, as in two cases, the body is invaded, while the head is not in contact with the tumor, inflammatory alterations occur only in the part of the gland distal to the point at which the duct is compressed. The carcinomatous tissue, moreover, acts as a local inflammatory irritant, and in its immediate neighborhood there is a proliferation of the gland stroma replacing the parenchymatous elements.

Ascending Infections from the Duodenum. Occlusion of the duct and stagnation of the pancreatic secretion produce conditions favorable for the invasion of bacteria. Under certain circumstances bacteria from the duodenum or from inflamed biliary passages may invade the pancreatic ducts in the absence of duct obstruction. In Case V. the inflammatory process was transmitted to the pancreas from the inflamed bile passages, though there was no evidence that the pancreatic duct had been occluded.

The following case is described in order to show that acute interstitial pancreatitis may accompany an acute inflammation of the stomach and duodenum, and is doubtless the result of an ascending duct infection:

Case of Acute Pancreatitis. The patient, female, aged thirty-eight years, was admitted to the service of Dr. Osler eighteen days before her death. She had had four children born at term and six miscarriages, the last a little more than a year ago. During her pregnancies micturition has been frequent and painful. Following the last her feet became swollen, and urination has been very frequent. Her appetite has been good, but she has been troubled with indigestion and has vomited frequently after meals. During her stay in the hospital the œdema of the legs, arms, and dependent parts increased. The urine contained a considerable amount of albumin (0.3 to 0.4 per cent.), and hyaline and epithelial casts. The patient died in uræmic coma on the nineteenth day after her admission.

[1] Journal of Experimental Medicine, 1901, vol. v. p. 409.

Anatomical Diagnosis. Chronic diffuse nephritis; small, granular kidneys; hypertrophy of the heart; general arterial sclerosis; chronic passive congestion of the viscera; acute and chronic gastritis and duodenitis; acute interstitial pancreatitis.

The stomach contains clear, viscid mucus adherent to the mucosa, which shows deep scarlet-red injection. In the duodenum, particularly upon the summits of the valvulæ conniventes, similar injection is seen. The pancreas is very firm in consistence. Microscopical examination of the stomach wall shows the superficial bloodvessels of the mucosa deeply injected, while between and within the glands polynuclear leucocytes are abundant. Between the glands plasma cells are present in large number. The alterations of the duodenal mucosa are of the same character, though slightly less marked. The interstitial tissue of the pancreas is œdematous and infiltrated with polynuclear leucocytes, often forming collections of considerable size. The ducts contain products of secretion and polynuclear leucocytes, often in abundance.

In the preceding case acute interstitial pancreatitis of moderate severity accompanied inflammation of the stomach and duodenum, which, associated with chronic nephritis and chronic passive congestion, had for several months before the patient's death caused frequent vomiting. The ducts of the gland contained inflammatory products, and the lesion was evidently the result of an ascending inflammatory process, having its origin in the gastro-intestinal tract.

Doubtless many cases of chronic inflammation are the result of a primary acute lesion, and represent a late stage of the process. This condition is illustrated by the following specimen, obtained from an autopsy not performed in the laboratory, and unaccompanied by clinical history or autopsy notes. It is described in order to show that proliferation of the interstitial tissue may follow an acute suppurative process. Beginning proliferation of the interstitial tissue accompanies acute inflammation, and the lesion may be said to be in a transitional or subacute stage. The process is doubtless caused by bacterial invasion, and numerous bacilli are demonstrable in the ducts and in the acutely inflamed interstitial tissue.

Specimen of Acute Interstitial Pancreatitis The interlobular tissue is œdematous, and contains scattered accumulations of polynuclear leucocytes, often in great number, among which are lymphoid and young fibroblast cells. The interlobular fibrous bands are slightly thickened, and here and there occur collections of lymphoid cells. The lumina of the acini are often dilated and contain polynuclear leucocytes. In specimens stained with methylene blue, short bacilli, varying in size, are found both in and between the acini where leucocytes are abundant and in large numbers within the lumina of the ducts.

Korte[1] has produced chronic inflammation of the pancreas by injecting Bacillus coli into the pancreatic duct, and has obtained a similar

[1] Berliner Klinic, 1896, No. 102.

result by injecting fecal material. By an ingenious method Carnot[1] produced conditions by which an ascending infection from the duodenum results. A thread was inserted into the pancreatic duct and through its orifice into the duodenum, and left fixed in this position. Advanced sclerosis of the gland resulted, and the walls of the ducts were thickened and infiltrated with leucocytes, while the interstitial tissue of the gland was much increased. In another experiment Carnot produced suppurative inflammation by injecting colon bacilli into the pancreatic duct.

Chronic Interlobular Pancreatitis Associated with Persistent Vomiting. In four cases advanced chronic pancreatitis has been found in cases which during life suffered with persistent vomiting. Two of these cases occurred in young women, and there was no history of syphilis, alcoholic excess, nor any other condition which has been assigned as a cause of chronic pancreatitis, and at the autopsy the ducts of the gland were found unobstructed. In one of these cases vomiting accompanied pregnancy, the clinical diagnosis being emesis gravidarum. The third case occurred in a man, aged forty-nine years, who, though once addicted to alcohol, had for ten years led a temperate life; chronic gastritis was found at autopsy. In the fourth case the condition accompanied constriction of the terminal part of the duodenum. In all of these cases the clinical history affords evidence of continued gastric or gastro-intestinal disease, namely, epigastric pain, nausea, and vomiting, the latter repeated and severe.

Case XI.—The patient, a deaf mute, female, aged thirty-one years, entered the service of Dr. Osler complaining of heartburn and dyspepsia. She states that at the age of twenty-four years she had "inflammation of the stomach," and was sick for eight weeks. She has had one living child and three miscarriages. She is at present pregnant, and has not menstruated for twelve weeks. For six or seven years she has had dyspepsia. Four days before her admission she began to vomit, the vomiting has persistently continued and has occurred irrespective of the taking of food. There has been no blood in the vomitus. She complains of a constant burning pain in the epigastrium, which is increased after eating. Physical examination disclosed nothing of importance. During the day, after her admission, vomiting was almost continuous, often occurring three or four times an hour. Examination of the vomitus showed a total acidity of 11, free hydrochloric acid 9; no lactic acid; hæmin crystals were present. The red blood-corpuscles numbered 8,612,000, the white corpuscles 17,000, hæmoglobin 125 per cent. In the afternoon of the following day, the patient becoming much weaker and semi-conscious, the vomiting ceased.

She was transferred to the surgical side, and an exploratory laparotomy was performed, but nothing was found to account for the symptoms. The patient's condition after operation was improved, and there

[1] Loc. cit.

was no return of vomiting until twelve days later, when it recurred with its previous persistence. The pulse was rapid and irregular, 112 to 152 to the minute. The vomiting ceased for a short time, but recurred a week later.

The patient was transferred to the obstetrical ward, and it was decided to empty the uterus. The cervix was dilated, and an ovum two and a half months old was removed. The patient rallied from the operation, but died on the twenty-second day after her admission. The urine contained a trace of albumin and a few hyaline casts, but at no time sugar.

Anatomical Diagnosis. Endometritis of puerperal uterus; anomalous artery, a branch of the aorta penetrating the substance of the right lung; rupture, with formation of cavity containing blood-clots; chronic interstitial pancreatitis.

The condition of the uterus and of the right lung will not be described. The stomach is normal, save for the presence of a few submucous ecchymoses; the duodenum is normal in appearance. The pancreas, weighing 75 grammes, is almost board-like in consistence; the surface is nodular and irregular, while on section the texture is homogeneous, the normal loose interlobular tissue being replaced by dense stroma. This interlobular tissue is dense and fibrous, and contains many spindle-shaped, lymphoid eosinophile and plasma cells. Entire lobules are at times partially destroyed, a few scattered acini remaining in the proliferated stroma, but in general the sharply defined lobules are not invaded by the process.

Case XII.—H. B., female, aged twenty-eight years, was admitted to the hospital, complaining of bleeding from the vagina, weakness, and pain in the abdomen. She had had chills and fever at the age of twenty years, and two years ago smallpox, but otherwise she had been healthy. Her present illness began ten months before her admission, with a sudden, profuse hemorrhage from the vagina, and since this time she had discharged clots of blood. An operation, the nature of which she does not know, was performed five months before, and was followed by much nausea and vomiting. Previous to her admission she has been much nauseated, and states that even a small quantity of water may cause her to vomit, so that though often hungry she is afraid to eat. The bowels are constipated. She has colicky pains in the epigastrium, and during the examination she frequently puts her hand to the umbilical region and complains of cramps. The patient was much emaciated and anæmic. Vaginal examination demonstrated the presence of an inoperable fungating carcinoma of the cervix. While in the hospital the patient's condition gradually became worse, and death occurred. The urine contained no sugar.

Anatomical Diagnosis. Carcinoma of the uterus, with metastases in the broad ligaments, pelvic and lumbar lymphatic glands, liver, and rectum; double pyelonephrosis; chronic interstitial pancreatitis.

The pancreas is firm in consistence, and on section very compact in texture, the interlobular tissue being replaced by denser stroma. There are no noteworthy changes in the stomach, intestine, or bile passages. Microscopical examination of the pancreas shows an abundant proliferation of the interlobular tissue, which is dense and fibrous, but often contains lymphoid and plasma cells in considerable number. It separates sharply the lobules, which are usually rounded as though compressed by the new tissue.

CASE XIII.—Male, aged forty-nine years, was admitted to the service of Dr. Osler, complaining of rheumatism, cough, shortness of breath, and indigestion. He had had three attacks of inflammatory rheumatism before the age of twenty-one years, but since has had fairly good health. He denies having had syphilis; he admits having formerly used alcohol in excess, but says that for the last ten years he has not been a heavy drinker, only taking a drink occasionally. He has been short of breath on exertion for five years; but indigestion, with which he suffers, troubles him, he states, even more than the shortness of breath. For a year past he has had attacks of vomiting without any apparent cause and with no relation to the taking of food, occurring sometimes in the morning before breakfast. He describes the vomitus as consisting in great part of phlegm. On admission, the patient is a well-nourished man, slightly cyanosed. The heart is hypertrophied, its action is feeble, and at the apex is heard a systolic murmur. On one occasion he passed a small amount of blood by the rectum. His condition gradually became worse, and he died on the fourth day after admission. The temperature while in the hospital was subnormal; the urine contained a trace of albumin, hyaline and granular casts, but no sugar.

Anatomical Diagnosis. Chronic endocarditis of the mitral valve; dilatation and hypertrophy of the heart; cardiac thrombi; chronic passive congestion of the viscera; infarcts of lungs; right hydrothorax; acute and chronic gastritis; ulceration of the ileum and colon; chronic pancreatitis with lipomatosis.

The mucosa of the stomach, covered by a thick layer of tenacious mucus, has a puffy appearance and is red in color, studded with small submucous ecchymoses. Superficially the pancreas appears to be a mass of fat, glandular tissue being nowhere visible; it weighs 152 grammes. On section the gland tissue is found to be in very great part replaced by fat. The duct of Wirsung is patent throughout, and about its branches can be seen small masses of reddish-yellow gland tissue embedded in fat, and forming, except in the tail, a relatively small proportion of the cut surface.

Microscopical examination shows that groups of lobules are widely separated by adipose tissue, while within these groups individual lobules are separated by thickened strands of dense stroma containing many lymphoid cells. In places are seen lobules in process of disintegration, dilated acini composed of cubical cells, being separated by new-formed stroma, but usually the new-formed tissue does not invade the lobules.

The cases just described demonstrate the occurrence of chronic interlobular pancreatitis in individuals who during life have suffered with persistent vomiting. They indicate the existence of some relationship between the underlying gastro-intestinal disturbance and the chronic lesion of the pancreas. It is improbable that persistent vomiting was caused by the pancreatic diseases, since in many cases the latter has existed unaccompanied by this symptom. Persistent vomiting, even though dependent upon disturbances of a reflex nervous mechanism, or upon the evacuation of toxic products into the stomach, is indicative of some profound change in the organ, and has apparently produced conditions

favoring an ascending infection of the ducts. The type of the accompanying pancreatic lesion favors this conclusion, since it is typically interlobular and resembles that observed in the preceding cases where infection of the pancreas had followed lesions of the gall ducts, with or without obstruction of the pancreatic duct. This explanation is further confirmed by the following case, in which persistent vomiting was the result of partial occlusion of the terminal part of the duodenum:

CASE XIV.—Mrs. F. G., aged fifty-one years, entered the service of Dr. Osler seven weeks before her death, complaining of nausea, vomiting, and loss of weight. Seven years before her uterus had been removed by Dr. Kelly for carcinoma of the cervix; she has since enjoyed good health. About six months before her admission she had noticed that she was losing weight. Later she was troubled with severe pain in the abdomen and back, uninfluenced by taking food, and became constipated. The pain disappeared, and she felt well until two months before entering the hospital, when she was attacked with very severe vomiting, occurring often five or six times a day and unaccompanied by nausea, but preceded by slight pains in the chest. Food caused no pain. Occasionally she passed several days without vomiting. Physical examination disclosed what appeared to be a tumor mass, irregular in outline, crossing the upper half of the umbilical region. While in the hospital there were frequently repeated attacks of vomiting, usually at intervals of twelve to eighteen hours, the vomitus consisting of greenish-yellow fluid material, varying in amount from a few cubic centimetres to a litre; it contained no blood. The patient gradually became weaker and died. The temperature occasionally rose to 100° F. The urine contained a small amount of albumin and a few hyaline and granular casts, but no sugar.

Anatomical Diagnosis. Recurrent adenocarcinoma of the retroperitoneal lymphatic glands and of the peritoneum; indurated retroperitoneal carcinomatous tissue, constricting the duodenum and left ureter; multiple abscesses of kidney; cystitis; bronchopneumonia; fatty degeneration of the liver; fibrous myocarditis.

There is no tumor mass in the pelvis, but in front of the sacrum, near the promontory, are a few enlarged firm lymphatic glands which, on microscopical examination, are found to contain an epithelial new-growth of the type of adenocarcinoma. On either side of the aorta occurs in moderate amount indurated tissue. Similar tissue, scar-like in character, is found at the base of the mesentery where the jejunum emerges, and upon the neighboring peritoneal surface are several small, soft nodules. Sclerotic tissue invading the wall of the duodenum at its termination has contracted the lumen to a diameter of twelve millimetres. The constricted area is not more than one centimetre in length, and above and below the intestinal wall is soft. From the base of the mesentery indurated tissue, which is found to consist of alveoli of epithelial cells embedded in dense stroma, extends into the mesentery of the transverse colon and in the retroperitoneal tissue as far as the left ureter, which is constricted by it. A narrow band of similar tissue extends between the pyloric end of the stomach and the pancreas, but does not invade the latter. The pancreas is very firm, and upon the surface individual lobules are sharply defined. The

ducts are not dilated. Microscopical examination shows an interlobular inflammation of moderate intensity, the lobulation being accentuated by thickened fibrous bands containing lymphoid, plasma, and eosinophile cells in fair abundance. The acini are dilated, the islands of Langerhans unchanged.

The four cases described show that chronic interlobular pancreatitis may occur as the result of alterations in the stomach and duodenum, which during life are manifested by long-persistent vomiting, and is presumably the consequence of an ascending infection of the duct. The mechanical effect of vomiting upon the ducts and their contents is obviously difficult to determine.

Alterations of the Bloodvessels. In the cases already considered, chronic pancreatitis has been secondary to alterations occurring in the ducts; in another group of cases the ducts are unchanged, and the lesion is referable to the bloodvessels or to toxic substances brought to the gland by the blood. In the pancreas, as in other organs, general arterial sclerosis has been thought to be the cause of fibroid induration, and G. Hoppe-Seyler[1] and Fleiner[2] have described cases of chronic interstitial pancreatitis attributed by them to obliterating endarteritis. Both writers think that changes in the vessels are followed by nutritive disturbances which cause degeneration of the parenchyma and its replacement by fibrous tissue. The condition, Fleiner suggests, is analogous to the contracted kidney, which is at times associated with general arterial sclerosis, and to changes in the liver, heart, and brain following arterial diseases. In three cases of arterial sclerosis Kasahara[3] found a moderate increase of the interstitial tissue of the pancreas, but in other cases of the same disease found nothing more than thickening of the bloodvessels. In none of the cases of chronic interstitial pancreatitis here considered has arterial sclerosis, general or local, been a conspicuous feature of the condition, and in only four cases was arterial sclerosis of moderate grade noted in the anatomical diagnosis. In two cases not included in the series the arteries of the pancreas were greatly thickened, while only in their immediate neighborhood was there proliferation of the interstitial tissue.

A second alteration of the bloodvessels assigned as a cause of chronic pancreatitis is chronic passive congestion. Friedreich[4] states that the lesion is not infrequently the result of long-continued venous gorging occurring in chronic diseases of the heart, lungs, and liver. The changes, he says, are usually slight, and do not cause destruction of the glandular elements, but between the acini are formed small tracts of thickened connective tissue, giving the gland an increased toughness.

[1] Deutsch. Archiv f. klin. Med., 1893, vol. lii. p. 171.
[2] Berliner klin. Wochenschr., 1894, vol. xxxi. pp. 5, 38.
[3] Virch. Arch., 1896, vol. cxliii. p. 111.
[4] von Ziemssen's Practice of Medicine (trans.), vol. viii. p. 551.

Small interstitial hemorrhages occur, and are changed later into collections of rust-colored pigment.

In the following case the pancreas was the seat of an extreme grade of chronic passive congestion following complete occlusion of the portal vein by a primary carcinoma of the liver.

CASE XV.—*Anatomical diagnosis.* Primary carcinoma of the liver, invading and occluding the portal vein; chronic passive congestion of the spleen, pancreas, stomach and intestines; ascites.

A large, carcinomatous mass occupies the right lobe of the liver and invades the branch and main trunk of the portal vein, which is greatly distended and wholly occluded. A plug of new-growth extends into the splenic vein. The pancreas is compressed by the distended vein behind it, and is firm and compact in texture and of a uniform dull brownish-red color.

In the head and body of the gland strands of carcinoma cells are found within the largest venules, at times wholly obliterating their lumen. In the immediate neighborhood fibrous tissue is increased in amount, and thickened strands extend between the lobules. At a distance from the carcinomatous tissue there is a very slight diffusely distributed increase of the interlobular tissue, which is denser than usual. Among the acini in places occur irregular patches of interstitial tissue poor in cells. Small hemorrhages have in places occurred into the interlobular tissue, and both here and within the secreting cells is found brown pigment. The bloodvessels are widely dilated.

In the preceding case the pancreas was the seat of a slight generalized increase of the interstitial tissue between the acini as well as between the lobules, but it serves to illustrate how small is the influence of chronic passive congestion in causing proliferation of the pancreatic connective tissue. In two additional cases of the present series chronic passive congestion dependent upon a valvular lesion of the heart accompanied chronic inflammation of the pancreas. One of these cases (Case XIII.) has already been described. In the following case the inflammatory change cannot with any certainty be attributed to chronic congestion, since at least one other possible factor existed, namely, lead poisoning.

CASE XVI.—H. D., a brass moulder, aged thirty-eight years, was admitted to service of Dr. Osler with symptoms of chronic lead poisoning and mitral stenosis. He disappeared from observation, and died four years later.

Anatomical Diagnosis. Mitral stenosis; dilatation and hypertrophy of the heart; chronic passive congestion of viscera; bronchopneumonia with gangrene; chronic interlobular pancreatitis, with fat infiltration; peripancreatic fat necrosis.

The frequency of chronic congestion of the abdominal viscera, and the relative infrequency of chronic interstitial inflammation of the pancreas, is evidence that the former condition is not commonly a cause

of the latter. Chronic passive congestion may doubtless produce slight proliferation of the interstitial tissue, but is an unimportant factor in the production of chronic pancreatitis.

In fourteen of the twenty-nine cases there is reason to believe that chronic inflammation has been the result of changes in the duct, obstruction, or ascending infection. In most of the remaining cases it is probable that the alterations present are like corresponding changes in the liver and kidney: cirrhosis, and chronic interstitial nephritis caused by the action of toxic substances present in the blood. Various conditions presumably capable of producing such substances have been assigned as the cause of chronic pancreatitis, and of these those notably worthy of consideration are tuberculosis, syphilis, and alcohol, named in the probable order of their increasing importance.

TUBERCULOSIS. Carnot[1] has recently directed attention to the occurrence of chronic pancreatitis in cases of tuberculosis. The specific lesion of tuberculosis is, he thinks, relatively uncommon in the gland, and in only one case has he observed acute miliary tuberculosis. Diffuse chronic interstitial inflammation of the pancreas, associated with tuberculous lesions of other organs is, he states, much more common, and a number of the older writers—Ancelet, Valpian, Arnozan and Morache—have cited such cases. Carnot examined the pancreas in patients dying with tuberculosis, and while in the majority no lesion was demonstrable, in seven cases he found a variable, usually moderate grade of chronic inflammation, causing in most cases an increase of the connective tissue normally present about the vessels, the ducts, and between the lobules. In five cases the lesion was associated with pulmonary tuberculosis, in one case with multiple tuberculous foci, presumably of the joints or of bone ("tuberculoses chirurgicales multiples"), accompanied by prolonged suppuration; while in one case a localized sclerosis of the splenic end of the pancreas accompanied an extensive tuberculous caseation of the left kidney. Carnot was able to produce chronic inflammatory changes in the pancreas of dogs, somewhat varied in extent and character, by injecting suspensions of tubercle cultures into the duct or into the parenchyma of the organ, but it was necessary to inject a very great quantity of the culture. A caseous abscess resulted in one case, but in the other experiments the lesion presented none of the specific characters of tuberculosis, and tubercle bacilli were not demonstrable in the tissues. In a single case localized sclerosis was produced by injecting into the parenchyma tuberculin extracted from the bodies of the dead bacilli.

In the two following cases chronic interstitial pancreatitis was found at the autopsy upon individuals dead with advanced tuberculous lesions.

[1] Loc. cit.

Case XVII.—H. G., male, aged thirty-one years, was admitted to the service of Dr. Osler, complaining of cough and weakness, with which he had suffered for about a year. Four months before his admission, for a week he had had much pain in the left side, and during the same time vomited every morning. He states that he has not had syphilis. The physical signs of an effusion into the left chest were present, and clear straw-colored fluid was removed by tapping. Evidence of partial consolidation of the left lung was obtained, and tubercle bacilli were found in the sputum. The patient rapidly became weaker, and died a month after admission. There had been no sugar in the urine.

Anatomical Diagnosis. Chronic pulmonary tuberculosis; tuberculous pleurisy, with hydrothorax on left side; tuberculous ulceration of larynx and ileum; bronchopneumonia; acute nephritis; chronic interlobular pancreatitis; fat necrosis about pancreas.

Upon the pancreas and in the omentum are a few opaque, white areas of fat necrosis. Microscopical examination of the pancreas shows a moderate grade of interlobular pancreatitis, and the lobules, more clearly defined than usual, are held together by thickened fibrous bands of compact tissue containing relatively few lymphoid cells.

Case XVIII.—H. B., female, aged seventeen years, was admitted to the service of Dr. Kelly. The present illness began a year before her death, with a profuse ill-smelling discharge from the vagina. Several months later she had fever, and since has not been well, complaining of pain in the back and abdomen. Vaginal examination, followed by curetting and histological examination of the material removed, demonstrated the existence of tuberculosis of the cervix uteri. The abdomen was later opened, but owing to numerous adhesions and abundant hemorrhage it was not possible to remove the uterus. Signs of tuberculous consolidation of the lungs subsequently developed and the temperature ranged between 99° and 103°. She died seven weeks after her admission. Sugar was not present in the urine.

Anatomical Diagnosis. Tuberculosis of the cervix uteri, endometrium, and Fallopian tubes; miliary tuberculosis of the spleen, kidneys, and liver; solitary tubercles of the cerebrum; tuberculous pleurisy; tuberculous ulcer of the rectum.

The pancreas is large and firm in consistence. There is a diffusely distributed increase of the interstitial tissue, most marked between the lobules, which are more clearly defined than usual. Lymphoid cells, plasma cells, and eosinophile leucocytes are fairly abundant in the new-formed stroma. In one section is found a miliary tubercle with a partially caseous centre.

In Case XVIII. the specific lesion of tuberculosis was found in the pancreas, but in Case XVII. tubercles did not occur in the specimens studied. In three additional cases in which tuberculous lesions were found in the pancreas there was no general proliferation of the interstitial tissue. The two cases described support the conclusions of Carnot that in a few instances generalized tuberculosis is accompanied by chronic pancreatitis, but they afford no explanation of its occurrence. The condition may be dependent upon the proximity of a tuberculous lesion, as in Carnot's case, where only the splenic extremity of the

gland in contact with a tuberculous kidney was affected, and a similar explanation may be applicable to the cases of Arnozan, in which chronic pancreatitis accompanied tuberculous peritonitis.

Since tuberculosis is, as is well known, a frequent complication of diabetes, its relationship to alterations of the pancreas are of much interest. In the cases just cited diabetes did not occur, and the lesion of moderate severity is interlobular, a type of inflammation accompanied by diabetes only when far advanced. There is, it appears, no reason to suppose that diabetes may be caused by pancreatitis resulting from tuberculosis.

Syphilis. The autopsy records of the Pathological Laboratory furnish no instance in which chronic pancreatitis has been associated with visceral syphilis, and, though the literature demonstrates that the two conditions occur in conjunction, acquired syphilis is certainly not the most common cause of the lesion, as Hansenmann,[1] Kasahara,[2] and other writers believe. In only one of the present series of cases was a history of syphilis obtained, and in this case chronic pancreatitis with formation of cysts was caused by primary carcinoma of the pancreas compressing the duct. In a case described by Drozda,[3] the pancreas was represented by a mass of indurated tissue in which glandular structures were recognizable only in the head, while here and there occurred caseous gummata embedded in the fibrous stroma. The liver was the seat of syphilitic cirrhosis, and the stomach contained an indurated scar. In a case of visceral syphilis, described by Chvostek,[4] the tail of the pancreas was penetrated by several sclerotic bands of tissue, giving it a lobed appearance. In these cases the alterations are analogous to syphilitic lesions of the liver, and are characterized by the occurrence of gummata or irregular, scar-like bands of tissue penetrating the parenchyma, and differ from the more common lesion in which there is a diffusely distributed increase of the interlobular or interacinar tissue. To the latter type belongs apparently the case of Dieckhoff,[5] in which, though there was a history of syphilis, coexisting carcinoma of the stomach and pulmonary tuberculosis may be regarded as possible etiological factors. In two cases of chronic interstitial pancreatitis associated with diabetes, Hansenmann obtained evidence of syphilis. Kasahara examined the pancreas in six cases of acquired syphilis, and in two found a moderate increase of the interstitial tissue, in two cases merely thickening of the bloodvessels, and in two cases no alterations.

Syphilis is, no doubt, a cause of chronic inflammation of the gland, and the cases of Drozda and Chvostek indicate the existence of a syph-

[1] Zeitsch. f. klin. Med., 1894, vol. xxvi. p. 191.
[2] Loc. cit.
[3] Wiener med. Presse, 1880, No. 31.
[4] Wiener med. Blätter, 1879, p. 791.
[5] Festschrift f. Thierfelder, Leipzig, 1895.

ilitic pancreatitis characterized by the occurrence of scar-like bands of tissue which may contain gummata. The etiological relationship of syphilis to a diffusely distributed interacinar or interlobular inflammation is more doubtful.

Alcohol. The common cause of cirrhosis of the liver is excessive use of alcoholic drinks. Cirrhosis is relatively infrequent when compared with the prevalence of alcoholic indulgence; but, as has been pointed out here, as with most diseases, other conditions are necessary in order that the disease results. Alcoholic excess is likewise regarded as a frequent cause of chronic interstitial pancreatitis, and in many instances a history of alcoholic indulgence can be obtained. Friedreich found at autopsy upon a drunkard chronic pancreatitis, cirrhosis of the liver, and granular kidneys. Chvostek, Dieckhoff, and Oser[1] have described cases in which cirrhosis of the liver and chronic pancreatitis were associated in alcoholics. In eight of the present twenty-nine cases a history of alcoholic excess was obtained, but in three of these cases (Cases I., II., and III.) chronic inflammation of the organ had followed obstruction of its duct by biliary or pancreatic calculi, and was indirectly, if at all, referable to the use of alcohol.

In the following case chronic interlobular pancreatitis, unaccompanied by cirrhosis of the liver, was found at autopsy in an individual dying with delirium tremens.

Case XIX.—J. M., male, aged fifty-three years, was admitted to the service of Dr. Osler with delirium. His wife, from whom a satisfactory history was not obtained, stated that he had been drinking very heavily for a month, and on the morning before his admission became delirious and feverish. The temperature was 101.5° F. The patient was in a talkative delirium, and there was tremor of the hands. The abdomen was distended and tympanitic. The patient became completely unconscious, the temperature rose to 105.4° F., and he died on the second day after admission.

Anatomical Diagnosis. Bronchitis and beginning aspiration pneumonia; acute diphtheritic and hemorrhagic colitis; fatty degeneration of the liver; chronic interlobular pancreatitis; fat necrosis near the pancreas.

The pancreas, of normal size, is very firm in consistence, and the interstitial tissue appears to be indurated. The ducts are normal. Numerous small foci of fat necrosis occur about the pancreas and in the transverse mesocolon. Microscopical examination shows a typical chronic interlobular pancreatitis, and the interstitial tissue contains numerous lymphoid cells.

Few reported cases of chronic inflammation of the pancreas not dependent upon lesions of the duct are described with sufficient detail to determine the presence or absence of an alcoholic history, and a review of them would afford statistics of little value. Alcohol being

[1] Die Erkrankungen des Pankreas. Nothnagel's Spec. Path. u. Ther., Vienna, 1898, vol. xviii.

the common cause of cirrhosis of the liver, the association of chronic pancreatitis with this lesion is significant.

Association of Chronic Pancreatitis with Cirrhosis of the Liver. The two conditions are frequently dependent upon similar etiological factors, since in the present twenty-nine cases of chronic pancreatitis cirrhosis of the liver was present in eight. In three of these cases pancreatitis was indirectly, if at all, related to the lesion of the liver, and had followed readily demonstrable changes in the duct of Wirsung. The relationship of the blood-supply of the liver to that of the pancreas suggests the possibility that venous obstruction might play a part in the production of pancreatic sclerosis, but the small influence which it exerts has already been pointed out.

Chronic inflammation of the liver and pancreas have been found associated by Friedreich, Chvostek, Hansenmann, Dieckhoff, Kasahara, Oser, and Lefas.[1] In six cases of chronic interstitial hepatitis Kasahara found a marked increase of connective tissue of the pancreas, in two cases a slight increase, and in two none at all.

Of considerable interest are the observations of Lefas, who studied alterations of the pancreas accompanying different varieties of hepatic cirrhosis. With the so-called atrophic or Laennec's cirrhosis he finds that the weight of the pancreas is often increased to 120 or 130 grammes, and the new-formed tissue, which is poor in cells, is uniformly intralobular, penetrating the parenchyma and isolating groups of acini. The point of origin seems to be the capillaries, but at an advanced stage there is a moderate grade of proliferation about the small veins and arteries. With hypertrophic biliary cirrhosis (of Hanot) there is no increase in the volume of the pancreas, but the interlobular tissue is increased in amount and in density, and, containing numerous cells, appears to have its origin about the ducts. The cases of interstitial pancreatitis which I have observed in part confirm the observations of Lefas, though a relationship of the newly-formed tissue to the blood-vessels and ducts was not evident.

In the following cases, previously reported[2] in greater detail, chronic interacinar pancreatitis accompanied by diabetes was associated with cirrhosis of the liver of the so-called atrophic type of Laennec.

Case XX.—The patient, male, aged forty-nine years, gave no history of alcoholic excess nor of syphilis.

Clinical Diagnosis. Cirrhosis of the liver, with congestion of the portal circulation and ascites; diabetes mellitus.

Anatomical Diagnosis. Atrophic cirrhosis (of Laennec); chronic interacinar pancreatitis; acute peritonitis, with effusion; splenic tumor.

The liver, which weighs 1370 grammes, has a rough, coarsely granular

[1] Arch. de Méd., 1900, N. S. 3, p. 539.

[2] Journal of Experimental Medicine, 1901, vol. v. p. 414.

surface, and on section shows a coarse network of thickened fibrous septa. The pancreas is small and firm in consistence. Microscopical examination shows a diffuse interacinar proliferation of the stroma invading the islands of Langerhans.

CASE XXI.—The patient, male, aged forty-seven years, gives a history of having used whiskey and beer in great quantity. For six months there have been symptoms of diabetes mellitus.

Anatomical Diagnosis. Atrophic cirrhosis (of Laennec); chronic passive congestion of the spleen; ascites; chronic interacinar pancreatitis; peripancreatic fat necrosis; general arterial sclerosis; gangrene of the leg.

The liver, diminished in size, is markedly hobnailed in appearance, and on section islands of parenchyma are isolated by thick strands of fibrous tissue. The pancreas, which weigh 108 grammes and is firm, presents microscopically a condition similar to that of the preceding case.

Numerous cases in which diabetes accompanied cirrhosis of the liver are recorded, and the relation of diabetes to diseases of the liver has been much discussed. It is probable that in such cases diabetes, as in the preceding cases, is dependent upon the coexistence of chronic pancreatitis, and cases with autopsy report described by Dieckhoff and Pusinelli[1] support this conclusion.

An excellent illustration of the dependence of chronic lesions of the liver and of the pancreas upon the same etiological factor is furnished by the disease of pigment metabolism, first described by von Recklinghausen as hæmochromatosis. In this condition an iron containing pigment is deposited in the cells of the liver, pancreas, and various other organs, and its presence is associated with death of parenchymatous cells and consequent proliferation of the stroma. The liver is the seat of an interstitial inflammation characterized by an increase of the connective tissue at the periphery and in the centre of the lobules. Though the liver is hypertrophied the histological picture resembles more closely the atrophic cirrhosis of Laennec than the so-called hypertrophic type described by Hanot. In Case XXII. of the present series (described in a previous article[2]) hæmochromatosis had resulted in the production of cirrhosis of the liver and chronic interacinar pancreatitis, resembling, though less advanced, the variety observed in the two preceding cases, but accompanied by deposition of an iron containing pigment, both in the secreting cells and in the newly-formed stroma. In the greater number of recorded cases of hæmachromatosis death has occurred with symptoms of diabetes mellitus, described by French writers as bronzed diabetes, since pigmentation of the skin is a conspicuous feature of the general pigmentation. In the present case diabetes mellitus was not

[1] Berliner klin. Wochensch., 1891, vol. xxx. p. 739.
[2] Journal of Experimental Medicine, 1899, vol. iv. p. 279.

present, doubtless because the lesion of the pancreas had not reached a sufficient grade of intensity.

In the following case hypertrophic cirrhosis of the type of Hanot was accompanied by interlobular pancreatitis.

CASE XXIII.—The patient, male, aged fifty-six years, admitted to the service of Dr. Osler, gives a history of having used whiskey in excess, usually taking from fifteen to twenty-five drinks a day. He denies having had syphilis. For the last year, until a short time ago, he has had attacks of vomiting, coming on without any relation to the taking of food; at one time about a year ago the vomiting was very severe. During the last six months he has become weak and short of breath. The conjunctivæ are slightly jaundiced. The liver is enlarged, the abdomen contains fluid, and the superficial veins are dilated. Three litres of bile-stained fluid were removed from the abdomen. Death occurred with increasing weakness nine days after admission.

Anatomical Diagnosis. Hypertrophic cirrhosis (of Hanot); ascites; chronic passive congestion of spleen; chronic interlobular pancreatitis; cholelithiasis.

The liver is greatly hypertrophied, weighing 2880 grammes; the surface is in places smooth, in places uneven and marked by low elevations, but without a hobnailed appearance. The tissue is firm and cuts with difficulty. Irregularly distributed bands and patches of fibrous tissue, rich in cells, separate ill-defined islands of parenchyma and penetrate between the cell columns and between individual cells. The gall-bladder contains many small faceted calculi. The pancreas, weighing 60 grammes, is very firm in consistence and evidently sclerotic. The duct of Wirsung in the body and tail of the gland is dilated and contains solid wax-like material. Microscopical examination shows that the lobules, particularly in the body and tail, are separated by dense sclerotic tissue showing little tendency to penetrate between the acini.

In the case just described so-called hypertrophic cirrhosis (of Hanot) was accompanied by interlobular pancreatitis, as in the cases observed by Lefas. In an additional case interlobular pancreatitis of moderate grade accompanied beginning cirrhosis, and, though the hepatic lesion corresponded to the so-called atrophic or Laennec's cirrhosis, the alteration of the pancreas differed from that observed by Lefas and found in Cases XX. and XXI. It is noteworthy, however, that the lesion was associated with tuberculous peritonitis, while a variety of chronic lesions coexisted in other organs.

CASE XXIV.—E. C., female, aged twenty-two years, was admitted to the service of Dr. Kelly with a fecal fistula following the removal of an abdominal tumor, the nature of which the patient did not know. An anastomosis was made between the sigmoid flexure and rectum. The patient died eight months later.

Anatomical Diagnosis. Invagination of the sigmoid flexure into the rectum; chronic periproctitis; fibrous adhesions uniting loops of ileum, with perforation of adjacent loops; perforation of a loop of the ileum

adherent to the abdominal wall, with formation of a fecal abscess and fistula; fibropurulent peritonitis; tuberculous peritonitis; tuberculosis of retroperitoneal lymphatic glands; chronic and acute endocarditis; chronic nephritis; cirrhosis of the liver with fatty degeneration; chronic interlobular pancreatitis.

INTERACINAR PANCREATITIS OF OBSCURE ETIOLOGY. In the present series of twenty-nine cases there are five instances of interacinar pancreatitis whose etiology is wholly obscure; in all of them the lesion is of very slight intensity. In four cases the islands of Langerhans were the seat of a remarkable hyaline change, and diabetes mellitus had resulted. I have already described one of these cases[1] in which, though the islands of Langerhans were almost uniformly affected by the degenerative change, increase of the interacinar stroma was very inconspicuous. Hyaline degeneration of the islands of Langerhans in association with diabetes has since proved to be of much more frequent occurrence than was at first suspected, and, in addition to the subsequent examples which have come to my notice, cases have been recently observed by Wright and Joslin,[2] and by Hertzog.[3] In one of two cases of Wright and Joslin, and in both cases of Hertzog, hyaline degeneration of the islands of Langerhans was associated with proliferation of the interstitial tissue of the gland.

In the following case the islands of Langerhans were almost wholly unchanged, but the pancreas was the seat of a slight interacinar pancreatitis, and diabetes was absent. The clinical and anatomical diagnosis in this case is as follows:

CASE XXIX.—Male, aged fifty-eight years.

Clinical Diagnosis. Inoperable carcinoma of the rectum; œsophageal diverticulum. Inguinal colostomy was performed, and later the œsophageal diverticulum, which compressed the trachea, was removed. Death followed the latter operation.

Anatomical Diagnosis. Carcinoma of rectum; metastases in the retroperitoneal lymphatic glands, liver, and lungs; colostomy wound; wound of operation for œsophageal diverticulum; bronchopneumonia; mucous polyp of the colon; chronic interacinar pancreatitis (slight).

Macroscopically the pancreas appeared unchanged, but microscopical examination shows the occurrence of thickened strands of connective tissue between the acini. The increase of interstitial tissue is, however, slight, and in many places is entirely absent. Only rarely are the islands of Langerhans implicated in the chronic inflammatory process.

Of eight cases of chronic interacinar pancreatitis, six were accompanied by diabetes mellitus. In those in which diabetes was absent,

[1] Journal of Experimental Medicine, 1901, vol. v. p. 527.
[2] Journal of Medical Research, 1901, vol. vi. p. 360.
[3] Transactions of the Chicago Pathological Society, 1901, vol. v. p. 15.

Case XXII., with hæmochromatosis, and Case XXIX., just described, the lesion was little advanced and the islands of Langerhans were only slightly affected.

Conclusions. 1. Chronic interstitial pancreatitis is slightly more frequent in males than in females. Two-thirds of the total number of cases occur between the ages of forty and sixty years.

2. The most frequent cause of chronic pancreatitis is obstruction of the duct of Wirsung, due to pancreatic calculi, to biliary calculi in the terminal part of the common bile-duct, or to carcinoma invading the head or body of the gland. Duct obstruction may be followed by the invasion of bacteria, which take part in the production of the resulting lesion.

3. Ascending infection of the unobstructed duct of Wirsung may follow an acute lesion of the duodenum or of the bile passages, and may cause chronic inflammation. In cases which have given a history of long, persistent vomiting, chronic diffuse pancreatitis may be found at autopsy, and is probably the result of an ascending infection of the gland.

4. General or local tuberculosis is occasionally accompanied by chronic diffuse pancreatitis, affecting chiefly the interstitial tissue of the gland.

5. Chronic interstitial pancreatitis is not infrequently dependent upon the same etiological factors, notably alcohol, which produce cirrhosis of the liver, and in about one-fourth of the cases the two lesions are associated.

6. Following duct obstruction and ascending infection the lesion affects principally the interlobular tissue, only secondarily invading the lobular tissue and sparing the islands of Langerhans. Diabetes results only when the lesion is far advanced.

7. Accompanying the so-called atrophic or Laennec's cirrhosis of the liver, the pancreas is at times the seat of a diffuse chronic inflammation, characterized by diffuse proliferation of the interacinar tissue, which invades the islands of Langerhans. A similar lesion accompanies hyaline degeneration of the islands of Langerhans and the condition known as hæmochromatosis.

8. Interacinar pancreatitis is usually accompanied by diabetes mellitus. When diabetes is absent the lesion is of such slight intensity that the islands of Langerhans are little implicated.

A NEW CABINET FOR MICROSCOPIC SLIDES, DESIGNED BY THE LATE THOMAS S. KIRKBRIDE, JR., M.D., OF PHILADELPHIA,

DIRECTOR OF THE POLYCLINIC LABORATORIES AND PATHOLOGIST TO THE POLYCLINIC HOSPITAL.

By Mary B. Kirkbride,
POLYCLINIC LABORATORIES, PHILADELPHIA.

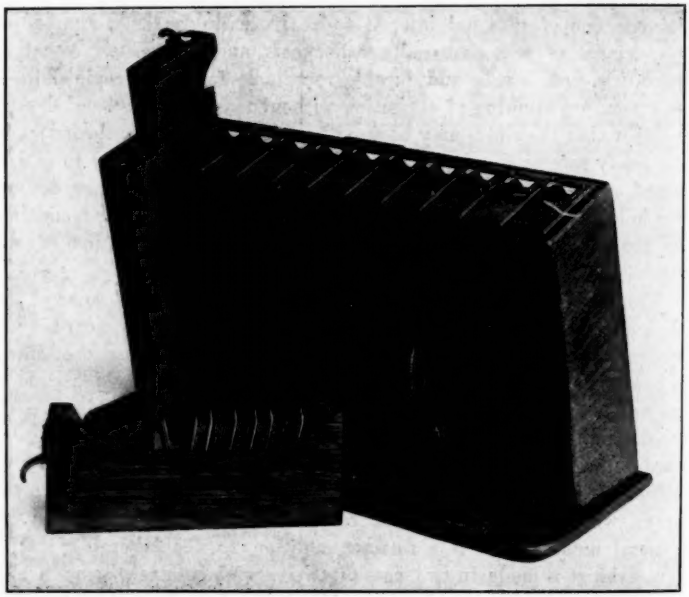
As scientific methods have come more and more into general use, the vexed question of how best to store and classify microscopic slides has become one of personal interest to an increasingly large number of physicians, as well as to all pathologists and biologists. What is needed is, first, a safe and durable receptacle for microscopic slides—compact, yet allowing of expansion without rearrangement, and so convenient that the slides may be used practically as well as theoretically for ready reference. And next, a working classification, easy to understand and use, yet comprehensive and uniform. Though new devices for holding slides and new methods for their indexing appear from time to time, there seems to be no entirely satisfactory solution of the problem.

The cabinet designed by Dr. Kirkbride attempts to meet some of the difficulties, and at the same time to adapt the methods of the card index system to the slides themselves. It consists of an oak case containing a row of narrow drawers or trays just wide enough to hold a slide in an upright position. On the front of each drawer is a combined label-holder and handle of brass. The slide box is patterned after the regular card index cases which are now found in almost every laboratory or office. It is strong throughout—notwithstanding the small size of the trays, which necessitates great care in their construction—and its general finish makes it a distinct addition to the laboratory outfit. The cabinet is made in two sizes of twelve and eighteen drawers, and as each drawer will contain about 110 slides of medium thickness, the cabinets hold (without guide cards) 1320 and 1980 slides, respectively. This is extremely compact, as the drawers are but 24 cm. (9½ in.) deep, and the length of the entire twelve-drawer case is not more than 49.5 cm. (19½ in.). When the large capacity and excellent workmanship are taken into account, the slide box will be found to compare very favorably in cost with others now on the market.

As shown by the illustration, the shell containing the drawers slants forward at an angle of 76 degrees. This makes the trays easier to handle and removes all danger of the slides falling out backward when the trays are taken out or put back, the front of the shell being used

as a kind of pivot upon which the drawer is steadied. The box is so arranged that the slides lie perfectly flat except while in use, and the thickness of the cardboard labels placed at both ends of the slides is just sufficient to prevent the slide above from touching the cover-glass of the slide below. The labels are made of the best quality of white bristol board, which gives an excellent writing surface; for fastening them to the slide, liquid fish glue has been found entirely satisfactory, as it hardens almost at once and holds permanently. The glue comes in convenient bottles, with a brush, and should be kept at hand on the

FIG. 1.



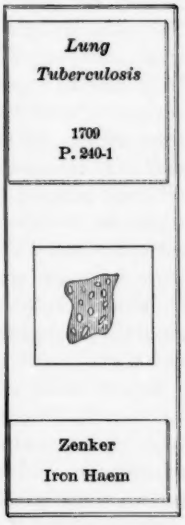
investigator's desk. It need hardly be added that the labels must be placed at both ends, or the slides would lie unevenly (see Fig. 2).

Since the cardboard is glued about 2 mm. from the ends of the slides, each at the top is separated from the next by a small space equal to the thickness of the label, which greatly facilitates "fingering over" the contents of a drawer. When the drawer is out the slides, as in the regular card index cases, slant slightly backward, so that by pushing forward the slide or slides in front the upper label can be read without taking the slide from the drawer. This slant, caused by the triangular block at the back of the drawer, is counterbalanced by the slope of the

shell, so that when the tray is in place the slides are flat. Besides the triangular block behind there is a second block in the front of each tray which is adjustable; thus it is possible to have the drawer partially filled, or to keep an approximate space for the final slides in any given classification.

The slides are their own index. Briefly, it is a "card index" system in which glass slides are substituted for cards, and the now unquestioned advantages of the card index apply with equal force to the slides; for no matter what classification is used, the collection may expand indefinitely, new slides being added in their proper places, or old ones removed without necessitating any rearrangement. Hence, it becomes a very simple matter to keep the collection "up-to-date" and in good order. Any specimen may be found at once, the label on the drawer and the guide card showing just where to look for it, and the necessity of a card index or reference book is avoided. This adaptability to rapidly growing collections makes the cabinet especially desirable for large laboratories.

FIG. 2.



The slide case lends itself to any system of indexing, such as decimal, alphabetical, or consecutive numbering. Dr. Kirkbride had spent much time and thought on the classification of pathological specimens, and at the time of his death was at work on a classification which he expected to publish in conjunction with the description of his cabinet. Unfortunately his plan was not perfected, but some general suggestions may prove helpful, the details being left to individual preference.

An alphabetical classification primarily under organs and secondarily under pathological conditions may be used in connection with the cabinets as follows: guide cards or slips are used of the best quality of bristol board, durable but light in weight, to economize space. Main divisions and subdivisions are distinguished by different colors. The slips are the same width as the slides, but project 5 mm. above them, so that the name of the division which each represents can be seen at once. White cards are used for the main or anatomical classification. Immediately behind each of these are slides showing normal conditions of the organ. Then follow blue guide cards in alphabetical order, similar to the white, but giving the pathological subdivisions. For example: Kidney (white card), Amyloid Degeneration (blue card), Inflammation (blue card), Tumors (blue card), etc. The same pathological changes may be present in almost all organs; therefore, the blue

guide cards will follow each main division in practically the same sequence. This uniform arrangement adds materially to the ease with which a slide is found. One slide, however, may present two or more pathological conditions, or several changes in a tissue, and cross indexing becomes necessary. Thus a section of kidney with both amyloid degeneration and inflammation should appear in two places. To obviate this difficulty a buff-colored cross index slip is used. The slide itself is placed under "Amyloid Degeneration," while its position and number are given on the cross index slip under "Inflammation." This same card gives references to all sections of kidney classified under other pathological changes, but also showing inflammatory processes. Or it may be expedient at times to keep together slides from a special case, such as an autopsy, even though they are from several organs and show various diseased conditions; here, again, the cross index card is used. In laboratories where the slides are consulted by a number of different persons, and there is danger of their being lost or mislaid, whenever a slide is taken from the collection for reference a salmon-colored removal slip should be put in its place. This gives the date when taken out and by whom, and any other necessary facts. Should a decimal classification be desired, the anatomical divisions would naturally be represented by the whole numbers, the pathological by the decimals.

Sets of blank cards are made by the manufacturers of the cabinet and may be obtained in packages containing fifty cards of one color. A simple but comprehensive working classification giving the main or anatomical divisions is in preparation and will shortly be printed on the white cards. The subdivision cards (blue) are left to be filled out as the character of the collection may require. To supplement the data given on the slides a regular card index is useful. The fixation, embedding, staining, etc., of each specimen are given and a short description of the finished section. Cards for this purpose have been specially ruled for the Polyclinic Laboratories; both these and the slide labels can be had from the makers of the cabinet.

The slide cabinet has now been in use in the Polyclinic Laboratories for over two years, and during that time it has been found thoroughly satisfactory. Thanks are due to Mr. W. E. Parker and Miss M. S. R. James, of Boston, whose interest and valuable suggestions have helped materially in the successful carrying out of Dr. Kirkbride's idea.

FURTHER STUDIES OF GRANULAR DEGENERATION OF THE ERYTHROCYTE.[1]

By Alfred Stengel, M.D., C. Y. White, M.D.,
and
William Pepper, M.D.,
of Philadelphia.

(From the William Pepper Laboratory of Clinical Medicine, Phoebe A. Hearst Foundation.)

In a previous communication, read at the meeting of the Association of American Physicians, held at Washington, April 29, 1901, and published in The American Journal of the Medical Sciences,[2] we presented our investigations of granular degeneration of the erythrocyte and in particular the facts bearing on the relations of this condition to lead poisoning. The material which we then accumulated gave us the opportunity to discuss the morphology of the condition and also its probable etiology. The direct dependence of the degeneration upon lead poisoning was shown by the regular occurrence of the granules in cases of lead poisoning admitted to the hospital, by the invariable discovery of the granules in men working in various capacities in lead works, by the discovery of granules soon after the administration of therapeutic doses in healthy individuals, and by the typical appearance of the corpuscles in dogs subjected to subacute or chronic lead poisoning. Further, we feel prepared to express a positive belief that the granular degeneration is the result of protoplasmic changes rather than the consequence of a nuclear fragmentation. We could see no relation between the granular condition and polychromatophilia excepting a frequent coincidence of the two conditions. Our belief was and remains that this granular condition is a true degeneration of an independent kind. We did not at that time feel prepared to state whether it occurs in lead poisoning as a result of the direct action of lead, or whether it is the consequence of anæmic conditions occasioned by the lead; nor did we then arrive at any conclusion as to the place of origin of the changes found in the circulating erythrocyte. The present communication has for its purpose: in the first place a further discussion of the probable nature of the granules, and in the second place the report of some observations made to determine, if possible, the location in which the changes take place.

To determine the place of origin of the changes, we studied the blood taken from different parts of the circulation as well as scrapings and preparations from the bone marrow and splenic pulp. The material was taken from four animals that had been kept under the influence of

[1] Read at the meeting of the American Medical Association, June, 1901.
[2] September, 1901.

lead for a considerable length of time. First, blood was taken from an artery and vein of the stomach, intestines, liver, spleen, and heart of etherized animals two hours after they had been given large doses of acetate of lead. The animals in each case had been under the influence of lead for some time, and granular erythrocytes were present in the circulating blood. The purpose of this experiment, which was prompted by Grawitz's view regarding the gastro-intestinal origin of the granular degeneration, was to determine whether erythrocytes showing this degeneration occur more abundantly in the blood of the portal vein and its tributary circulations than elsewhere. In only one of our experiments could we recognize an unequal distribution of granular cells. In this case more granular erythrocytes were found in the veins of the spleen, liver, and intestines than elsewhere. We, of course, cannot pretend that this single experience is of much weight in deciding the matter under discussion.

The bone marrow and spleen were examined in two ways: (*a*) By preparing spreads made from scrapings of the cut surface of the organs, and (*b*) by embedding portions of the organs, hardened in various ways, in paraffin, and sectioning. In the spreads granular erythrocytes, both nucleated and non-nucleated, were easily demonstrated, but were not more abundant than in the circulating blood. Fixation by heat and in mixtures of ether and absolute alcohol and in absolute alcohol and 1 per cent. formol gave the best results, heat being by far the most satisfactory. The sections did not in any case show granular cells, as the red corpuscles were more or less crenated, whatever the method of fixation. We could not, therefore, be certain of the presence or absence of granular erythrocytes.

The result of these experiments then gave us no indications of the probable place of origin of the granular degeneration. In no instance did we find more abundant granular cells in the bone marrow or spleen than in the peripheral blood.

Some experiments seemed desirable to determine whether the granular cells existed in the circulating blood or whether, on the other hand, they are artefacts. The characters of the granules, the regularity of their occurrence in the blood in certain diseases, as well as their discovery in scrapings of tissues had convinced us that the granular corpuscles are not artefacts, and the question has not been seriously raised. Nevertheless, we thought it advisable to practice injection of certain stains to determine whether the fresh blood-corpuscles after such injections would show granular cells. Dogs that had been kept under the influence of lead until the blood showed granular erythrocytes in abundance were etherized, and solutions of methylene blue or neutral-roth in 0.8 per cent. NaCl solution were injected into a vein. Specimens of blood were taken at various intervals of time from the

ear and examined fresh or after drying and fixation. The injections of methylene blue gave the only positive results. The blood in the successful cases showed nucleated and non-nucleated erythrocytes containing pale blue granules. The appearances of these granular cells were in every respect identical with those of the granular cells seen in stained spreads of the blood obtained before the injection of methylene blue, excepting that the staining of the granules was a little less intense. We could not confirm the observation of Sabrazes, Bourret, and Legér that the granules are eccentrically situated and show a tendency to extrusion.

The dried specimens of blood prepared as above described showed exactly similar conditions.

We have made a few attempts at artificial production of granular degeneration outside the body, and refer to them here, though we are aware of their unsatisfactory character. Quantities of human blood and of dog's blood were mixed with blood serum of dogs that had been under the influence of lead for some time. In no case did we reach positive results. The rapid disintegration of the red corpuscles under such circumstances naturally renders the experiment of little practical value. Equally unsatisfactory results attended the mixture of human blood and dog's blood with various solutions of acetate of lead. Sabrazes, Bourret, and Legér attempted to produce the degeneration by injecting solutions of lead into a ligated vein of a dog's leg, but without success.

A study of the various pathological conditions in which granular degeneration of the erythrocytes occurs seemed to us of possible importance in elucidating the question of the place of origin of the degeneration, and perhaps also its nature. Such a study is of course of even greater and more immediate interest in determining the diagnostic value of this reaction of lead poisoning. We therefore studied a considerable series of cases representing various diseases, and will refer to our results under the headings—chlorosis, pernicious anæmia, leukæmia, and miscellaneous medical and surgical diseases. The results obtained show that no explanation of the nature of the degeneration or its place of origin could be reached in this way.

Chlorosis. Contrary to the experience of other observers, we have found granular erythrocytes quite frequently in this disease. Among 18 cases examined by us there were 11 in which the granular cells were abundant. In 6 of the 11, the granules were fine; in the other 5 they were fine and occasionally coarse. In only 1 of the cases were the granules numerous. In this case the hæmoglobin was only reduced to 50 per cent., while in most of the cases a far greater reduction was noted. In all of the 11 cases polychromatic cells were seen, but these seemed to bear no relation in intensity or number to the granular cells.

Pernicious Anæmia. Judging from the seven cases which we observed, and from the reports published by others, granular degeneration is a constant condition in advanced stages of pernicious anæmia. We found the granules fairly numerous and at times very large and conspicuous. Though, however, in the number and the character of the granules the blood of pernicious anæmia was usually distinguished from that of other diseases, we did not often find in pernicious anæmia the extraordinary number and variety of granules, coarse and fine seen in nearly all of the cases of lead intoxication which we have examined; and the other characters of the blood would render a differentiation easy.

Leukæmia. We examined ten cases of this disease and found granules in every one, though they were usually fine and not present in large numbers. We shall have occasion to refer again to this matter, as the occurrence of the granules in leukæmia is of particular importance in connection with the determination of the nature of granular degeneration, nucleated erythrocytes being so abundant in this disease and nuclear degenerations of all kinds so frequent. We should look then to this disease more than in any other for a confirmation of the view that granular degeneration results from fragmentations of the nucleus.

Miscellaneous Medical and Surgical Diseases. In addition to the 35 cases above referred to, we have examined the blood in 105 patients in the medical and surgical wards of the University Hospital, and have discovered granular erythrocytes in 34 of these cases. In the 34 cases the diagnoses were as follows: typhoid fever, 3 cases; valvular heart disease, 3; peritonitis, 3; septicæmia, 3; tuberculous arthritis, 2; malaria, 2, and pertussis, heart disease and nephritis, lobar pneumonia and pleurisy, phthisis, malignant endocarditis, aneurism and nephritis, nephritis and anæmia, splenic anæmia, secondary anæmia, pseudoleukæmia, chronic diarrhœa, phlyctenular conjunctivitis, orchitis, carcinoma of stomach, lymphoma of neck, sarcoma of neck, empyema, osteomyelitis, each 1 case.

Several observers have reported the discovery of granular red cells in cases of sepsis, and, though the direct bearing of septic infections upon the conditions has not been established, it is of interest to note that this condition was present in some of the cases enumerated above. Perhaps half of the above 34 cases were more or less septic. In the other half of the cases there was no such element, but the high grade of anæmia may have been alone operative in these. In several of the cases no clue whatever to the causation of the granules could be found. We might speak of them as accidental occurrences, but this would not serve as an explanation. In none of the 34 miscellaneous cases were the granules abundant or conspicuous. Two instances in which the

blood picture approached that found in lead poisoning were a case of phlyctenular conjunctivitis in a boy, and a case of chronic diarrhœa in a man who had possibly taken acetate of lead in the treatment of his condition before he came under our observation. Even in these two cases we could easily distinguish the blood from that of lead poisoning, and in the remaining 32 cases the comparative sparseness of the granules and their finer character made the distinction very easy.

There were 71 cases in which we did not find granules. Some of these may be mentioned for the sake of showing that the classes of diseases in which the granules occur or do not occur give no indication of the probable source of the granular cells; and also to show that the condition of the blood as to infection or anæmia will not alone explain the degeneration.

We failed to find any granules in the following cases: 5 cases of valvular heart disease, 4 of phthisis, 4 of appendicitis, 7 of typhoid fever, 5 of sepsis, 6 of grippe, 3 of carcinoma of the stomach, 3 of diabetes, 2 of pneumonia, and in one case each of malaria, splenic anæmia, glanders, actinomycosis, and tetanus.

With the single exception of lead poisoning, no condition that we know of regularly causes this change, though other conditions operate to this end in occasional cases. As far as lead is concerned, we may refer again to our previous studies. In each of seven clinical cases of plumbism we found enormous numbers of the granular cells; and we may add six recent instances. In twenty-one men working in lead works, but showing no symptoms of lead poisoning, the granules were always found, but in varying numbers. Two of these men had worked in the lead works only four days. Moritz found the granular cells in six men working in lead works, but having no symptoms; and other observers, as Strauss, Grawitz, Behrendt, Sabrazes, Bourret, Legér, and Hamel (the last in 25 cases) found the granules in cases of lead poisoning. Strauss also discovered them in atropine poisoning and in rabbits and frogs poisoned with pyrodine. Kaminer and Rohnstein found granular cells in the blood of rabbits poisoned with phenylhydrazin on the fourteenth day of the intoxication. Sabrazes, Bourret, and Legér refer to a case of fatal copper poisoning in which numerous granules were found, but they failed to produce the degeneration in guinea-pigs by intraperitoneal injections of various toxic and non-toxic substances, such as distilled water, thallium acetate, carbonate of lithium, and sulphate of atropine, or by inhalations of nitrite of amyl, pyrodine, and phenyl hydrazin. Injections of lead acetate, however, caused the degeneration very rapidly in guinea-pigs as well as in rabbits. In our own experiments we have found the degenerations after poisoning a dog with potassium chlorate; the granules did not appear until shortly before death, but became very numerous. Another

dog slowly intoxicated with corrosive sublimate showed only a few granules shortly before death. They were also present in large numbers in the blood of dogs kept under the influence of toxic doses of pyrodine for many days. It is evident, therefore, that toxic causes of various sorts are capable of producing the granular degeneration we are studying, but it is equally evident that no poison thus far studied is as regular in its production of the degeneration or as prompt in its action as is lead.

The discussion of the nature of the granular condition of the red corpuscles has divided observers into two groups: those holding that the granules originate from the nucleus, and those who regard them as the product of a specific degeneration of the protoplasm.

The former view was the one first put forward after the granular cells were recognized, and has been lately defended by Askanazy, Lazarus, Engel, Litten and Strauss. These authors look upon the granules as the result of nuclear fragmentation—karyorrhexis—and they believe that it is the means by which the nucleated cell normally loses its nucleus before becoming an adult cell and entering in the peripheral circulation. The attractiveness of this theory is largely dependent upon its adaptability as an explanation of the disappearance of the nucleus, a matter which has remained unsolved in spite of painstaking examinations of histologists; but more definite facts are required to establish the truthfulness of the theory. It would seem entirely reasonable to expect blood pictures showing a gradual transition from the state of normal nucleated cells to that of erythrocytes containing scattered granules, but without a nucleus. As a matter of fact, Litten claims that he has seen direct transitions from the normal nucleus to fully granular cells, both in the circulating blood and in the bone marrow, and he states that the nucleus gradually becomes paler as the granules increase in number and size. Somewhat similar statements are made by Ewing. Litten's observations were made in only one case, a rapidly fatal one of pernicious anæmia. Our own observations have included a large number of cases of intense anæmia and of various intoxications, both clinical and experimental, and we have found in these abundant granular cells in the circulating blood as well as in the bone marrow and other organs, but we have never in a single instance among the thousands of granular cells that we have carefully examined found the slightest suggestion of a nuclear fragmentation productive of granulations. We have repeatedly found and figured, from paintings by an artist and from photographs, associations of nuclei and granules, that is, we have recorded the occurrence of granules in nucleated cells; but in every instance the periphery of the nucleus has either been clear-cut as in the normal nucleated cell, and the chromatin of the nucleus has presented normal appearances, or when degeneration has been

present there has been nothing suggesting even remotely an origin of granules in degeneration of the nucleus. The conditions in the blood of leukæmia seems to us to be particularly important in this connection. Nucleated erythrocytes with and without granules were very abundant in some of the cases studied, and in the same cases we often found evidences of nuclear degenerations, both in the white and in the red corpuscles. In no instance, however, could we see evidence of a transition of nucleated cells to granular cells.

If the theory of the gradual fragmentation of the nucleus were established, we should expect the evidences of such fragmentation to be most abundant in the bone marrow, where nucleated cells become non-nucleated; but our experience has been that the nucleated cells and the granular cells in bone marrow have been exactly the same as those of the peripheral circulation.

An observation made by us in several instances of still greater significance to disprove the nuclear origin of the granules was the discovery of karyomitosis in granular erythrocytes. One observation of this sort seems to us more valuable than any amount of negative evidence or of theorizing. It is unlikely that a nucleus could at the same time be in a state of active mitosis and of karyorrhexis.

The second theory regarding the nature of the degeneration, and the one to which we incline, is that which has been defended by Grawitz, Moritz, Hamel, and Bloch, and which attributes the granular condition to a peculiar protoplasmic degeneration. In the consideration of this theory we would first of all direct attention to the fact that all of the protoplasmic degenerations of erythrocytes that have been thus far described are characterized by the development of a basophilic tendency. Thus, in the studies of Maragliano and Castellino particular attention was directed to this peculiarity of the degenerated areas, and the behavior of polychromatophilic cells, so generally considered degenerative, is very similar. In no case is there the distinct basic affinity of the degenerated parts of the cell that is seen in the granular degeneration under consideration, but this is a point of too little importance to disprove our view.

Grawitz did not consider the granules the results of nuclear fragmentation, because in his earlier work he had not seen these granules in nucleated red corpuscles. He had expected to find them if these granulated cells were the unfinished red cells prematurely placed in the peripheral circulation. Under such circumstances granular nucleated red corpuscles should be found, or at least transitional forms should occur. Later he found nucleated erythrocytes with these granules in the protoplasm, but the nucleus was to all appearances normal. This last observation induced him to study the blood-forming organs, but here he was unable to see any evidence of these granules. From these

observations he came to the conclusion that the granules are the result of degenerative processes in the hæmoglobin, caused by poisons acting directly upon the erythrocytes, and suggests that this takes place outside of the blood-forming organs.

Our own studies have shown granular nucleated erythrocytes in the peripheral blood, and also granular erythrocytes, nucleated and non-nucleated, in the bone marrow; but, like Grawitz, we have failed to find any transitions from the non-granular nucleated erythrocytes to the granular non-nucleated cell. While the proof of the protoplasmic origin of the granules is therefore more or less negative or indirect, we believe the evidence against the nuclear origin of the granules is direct and positive. This evidence may be summarized as follows:

1. Karolytic and karyorrhexic changes may be observed in nucleated red cells without showing any granular change in the protoplasm of the cells; on the other hand, granular degeneration may accompany these nuclear changes without association of the nuclear and granular processes.

2. The granulated red cells (coarse or fine granules) never show the remains or a suggestion of a former nucleus.

3. The granules are observed in karyokinetic red cells, and we have seen them associated with the several stages of the dividing nucleus. We cannot believe that such a progressive and retrogressive change can be present in the nucleus at the same time, without internal evidence of degeneration.

4. The very early appearance of these granules in the blood taken from the peripheral circulation (twenty-five hours after a dose of 7½ grains of the acetate of lead has been taken by one of us) to a certain extent indicates a probable beginning of the destructive changes in the erythrocytes (non-nucleated) of the peripheral blood, rather than in the erythrocytes (nucleated) at the moment in process of formation in blood-making organs.

5. The granules observed in the bone marrow were absolutely the same as those seen in the peripheral blood. Those in the nucleated cells, chiefly normoblasts, showed no evidence of derivation from the nucleus, the nuclei being in each case normal in size, shape, and staining qualities and like those of the neighboring nucleated cells which did not contain granules.

6. Finally it seems to us that in certain cases of leukæmia in which great numbers of nucleated red cells are always present, if these granules were nuclear derivatives, distinct steps or transitions could be demonstrated. Such is not the case. On the contrary, distinct degenerative changes, karyorrhexis, karyolysis, pyknosis, atrophy of the nucleus, etc., are present sometimes with and sometimes without granular protoplasm; but there are never in our experience any

transitional stages to indicate gradual destruction of nuclei with liberation of substance that has gone to form granules. In addition very many of the nucleated cells showing nuclear degeneration contained no granules.

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THE LATERAL CHAIN THEORY OF EHRLICH AS EXPLANATORY OF TOXINS, ANTITOXINS, BACTERIOLYSINS, AND HÆMOLYSINS.

BY F. P. GAY, M.D.,
ASSISTANT DEMONSTRATOR OF PATHOLOGY, UNIVERSITY OF PENNSYLVANIA.

THE last three years of Continental activity have added so much to our knowledge of the blood in both normal and immunized animals that a retrospect and conclusions by the one who has been most closely identified with progress along these lines is particularly grateful. Ehrlich in several recent communications has reiterated his "lateral or side chain" theory as explanatory of toxins and antitoxins, and found new data in his and others' works on bacteriolysins and hæmolysins from which he has enlarged and made more conclusive this admirable theory of cell mechanism.

TOXINS AND ANTITOXINS. Toxins are labile, poisonous substances, elaborated by plant and animal cells, of which we have no exact chemical knowledge, but whose characteristics are recognizable by their physiological effect on animals. Toxins differ from all known chemical poisons in these important particulars: 1. They are subject to cell assimilation, that is, they enter into direct chemical combination with protoplasm, whereas chemical substances either destroy the cell or are present in it in solution. 2. Toxins can call forth the production of antitoxins in the animal body, while chemical poisons cannot. 3. The action of toxins is delayed by a considerable incubation period.

Toxins which have undergone change by time or certain chemical substances form substances known as toxoids, which possess an equal power of stimulating the formation of antitoxins, but have relatively little toxic effect.

Antitoxins are substances formed in the animal body by the inoculation of toxins or toxoids; they are recognized by their action in neutralizing the effect of toxins. It was at first supposed by some that these bodies were direct reaction products of toxins, but Knorr soon showed that one unit of toxin gave rise to an amount of antitoxin sufficient to neutralize 100,000 such units—a disparity inconceivable in a process analogous to a chemical reaction. The variation in duration of active and of passive immunity, the presence of normal antitoxic bodies, and the increased production of antitoxin under the action of pilocarpine are all observations which make it certain that antitoxins must be regarded as products of cell activity. Roux, Metchnikoff, and others maintained that the neutralization of toxin by antitoxin is due to a stimulation of somatic cells, more particularly the phagocytes of the circulating blood, which enables them to counteract the poisonous effect of the toxins. But it has been shown by Madsen, Ehrlich, and C. J. Martin that the neutralization will take place *in vitro* irrespective of the presence of animal cells. This chemical form of neutralization of the toxins, together with the whole explanation of the formation of antitoxins, is reasonably and adequately accounted for by Ehrlich's "lateral chain" theory, as will be seen.

Virchow pointed out in his *Cellular Pathology* that chemical substances were picked out by certain organs. The almost absolute absorption of the toxins of tetanus and diphtheria by nerve cells are further instances of the elective action. The obvious example of the variation of leucocytes in their reaction to stains is but a further step in cell differentiation. It is on this basis of finer cell structure, as suggested to us, that Ehrlich has conceived each cell as possessing, in addition to its nucleus, multitudes of atomic "lateral chains" or "receptors," each with its affinity for a certain assimilable substance. The normal function of the receptors lies principally in this choice of suitable foodstuffs, but toxins as assimilable substances are also taken up by receptors fitted for the purpose.

The toxin unit must now be considered as more than a simple body; it possesses, in fact, at least two parts, a "haptophore" group, which unites it to the cell receptor, and a "toxophore" complex, which is the poisonous element. Toxoids as altered toxins possess only the haptophore group, which accounts for their absence of toxic effect. The body cell is more or less injured if the united unit be a toxin,

owing to the toxophore group; but even if there be no toxophore group present, as in a toxoid, the receptors united are thrown out of function. Loss of the cell constituents in either case leads to regeneration of the parts affected, and regeneration of tissues, as Weigert has shown, takes place always in excess. This excess of toxin elective "receptors" cumbers the cells, and they are eventually thrown off into the circulating blood, where they form the antitoxins. A toxin cannot harm a cell unless its haptophore group unites with a cell "receptor;" when "circulating receptors" or antitoxins are present in the blood the haptophore groups become anchored and never reach the cell, which accounts for the neutralization of the action of toxin by antitoxin. Absence of "receptors" suitable to unite with toxins explains the natural immunity of certain animals to certain toxins. Predominance of suitable receptors accounts for the election of certain toxins by certain tissues. A multiplicity of toxic bodies such as may occur in a single bacterial toxin simply calls for a corresponding multiplicity of receptors.

The period of incubation is the time during which the "receptors" are regenerating in the cells and before they are thrown off into the circulation. That the origin of antitoxins is primarily in the fixed cells is further shown by the fact that organs acquire antitoxic properties before the blood itself.

"Receptors" which unite with toxins are called "receptors of the first order," being relatively simple and having only one receptive process. Similarly toxins are "uniceptors," that is, they have only one uniting arm, the haptophore group. This conception is better understood on comparison with the structure of the hæmolysins and their "receptors."

Bacteriolysins and Hæmolysins. In 1894 Pfeiffer noted when the living vibrios of cholera were mixed with the serum of animals immunized against cholera, and the mixture injected into the peritoneal cavity of a normal guinea-pig, that within an hour the bacteria were broken up and destroyed, that is, bacteriolysis had taken place. Metchnikoff soon showed that this could be produced *in vitro* with immune serum which had been kept for some time, provided that the fresh peritoneal exudate of a guinea-pig were added. Bordet then showed that agglutination and bacteriolysis would take place with fresh immune serum alone. With serum which had stood for some time or which had been heated to 55° C., for twenty minutes, however, the power of bacteriolysis was lost, while agglutination was retained; and then, curiously enough, he found that the addition of fresh serum of a normal animal would restore the bacteriolytic power. From these data it was easy to conclude that bacteriolysis depends on two elements: first, a

specific body acquired by immunization which is not destroyed at 55° C.; and, second, a substance present in all normal sera, destroyed by heat or by standing. A similar bacteriolytic power which frequently occurs in normal sera only shows that a natural immunity exists to a certain extent.

It has long been known that the serum of certain animals has the power of breaking up or hæmolizing the red blood-corpuscles of other animals, causing the opaque solution of normal defibrinated blood to become laky and transparent by the dissolving out of the hæmoglobin from the discoplasm. Such occurrences give rise clinically to the accidents of transfusion. It was shown first by Belfanti and Carbone, and later, in 1898, by Bordet, that this hæmolytic power can be artificially produced in practically any animal. If, for example, a guinea-pig is inoculated with the red blood-corpuscles of a rabbit, its serum soon acquires a marked power to agglutinate and hæmolize the rabbit's red blood-corpuscles. In parallelism with the power of bacteriolysis, guinea-pig's serum hæmolytic for rabbit's red blood-corpuscles loses its power when heated to 55° C. for twenty minutes, and regains it when normal, fresh, guinea-pig serum is added. To the analogous immune bodies in bacteriolytic and hæmolytic sera Bordet gave the name of "substance sensibilisatrice," from his conception of it as acting merely as a fixative agent which renders it possible for the thermolabile substance, the "alexine," to attack and destroy the cell. This use of the word "alexine" is confusing, as the same name has been used by Buchner to indicate the substance causing bacteriolysis before this causative element was shown to be composed of the two substances mentioned above.

Ehrlich was able immediately to confirm Bordet's experiments, but instead of accepting the latter's conclusions, showed at once the relation of hæmolysis to—and its confirmation of—his already elaborated lateral chain theory. Both from his own data and conclusions, and from the experiments of Bordet and others, Ehrlich in the past few years has developed a concept fascinating in detail and increasingly more convincing.

As already shown, a hæmolytic serum contains two substances, to which Ehrlich has given the names of "immune body" and "complement." The immune body has two affinities, a stronger one for the red blood cell, and a weaker one for the complement. At 0° C. the immune body will unite with the red blood cell, causing no hæmolysis, and leaving the complement free in the solution. The union can be proved by repeatedly washing in normal saline the centrifuged red blood-corpuscles to get rid of all complement, and then adding at room-temperature fresh normal serum containing complement alone; hæmo-

lysis takes place, showing that the red corpuscles contain a united immune body.[1]

The immune body having two uniting processes is an "amboceptor." The complement resembles in its constitution and action a toxin; it has a haptophore group, which unites with the immune body, and a "zymotoxic complex," which acts on the red blood cells saturated with immune body in a manner partially toxic and partially fermentative. The complement can unite with red blood-corpuscles only in the presence of the immune or intermediary body. Just as the inoculation of toxins gives rise to antitoxins, so inoculations with "hæmolysins" give rise to antihæmolysins, which are more complex, however, being composed of "anticomplements" and "anti-immune bodies." There is reason to suppose that although the heating of hæmolysins destroys the action of the complement, that in reality it is not wholly destroyed but forms a "complementoid," which, as in the case of toxoids, can form anti-complements.

We have seen that receptors of the first order have but one haptophore group, which in the case cited united with a toxin. Red blood cells, in common with other cells, contain these receptors of simpler structure, and, in addition, "receptors of the second order" with which we have to deal in the phenomena of hæmolysis.[2] Receptors of the second order have two haptophore groups, one of which unites with a nutritional substance (immune body), and the other with a fermentative substance (complement). That these receptors occur in excess, at least in the case of hæmolysis, is shown by the fact that the red blood cells in the absence of complement will fix many times the amount of immune body necessary for complete hæmolysis. The reproduction and throwing off of these receptors gives rise to amboceptors in the blood, in the instance which we are following, to antihæmolysins. And in general it may be said that any substance which has one or more haptophore groups can give rise to antibodies, which are either uniceptors or amboceptors, depending on the number of haptophore groups in the causative substance.[3]

The formation of antitoxins by means of toxins, bacteriolysins by means of bacteria, hæmolysins by means of red blood-corpuscles, is

[1] The immune body, on account of its acting position between the complement and the red blood cell, is also referred to as "intermediary body."

[2] Ehrlich, in the "Schlussbetrachtungen," adopts a slightly different classification. In this communication only he has referred to the receptors mentioned above as "receptors of the third order," and interpolates another class. The function of these other receptors is that of breaking up the more complex nutritional molecules, for which purpose they possess two arms, one, a haptophore group to unite with the molecule, and the other a "zymphoric complex," which exerts a fermentative action on the attached substance.

[3] Ehrlich has of late used the term "haptines" to denote in general any thrown-off receptors.

but the overproduction of normally existing cell elements. Natural immunity is but an expression of a relatively large number of such preformed elements. Furthermore, each complement, each immune body, and so forth, is individual and gives rise to a specific antibody. That a certain interaction of relatively specific substances is possible is easily explainable. For example, isohæmolysins are producible, that is, hæmolysins acting against the blood of other animals of the same species; but they will hæmolize the red blood-corpuscles of only certain of these animals, namely, of those having red blood-corpuscle receptors very similar to or identical with the receptors of the blood giving rise to the hæmolysins. Incomplete hæmolysis is, perhaps, due either to merely similar receptors or to an insufficient quantity of identical receptors. Bordet has steadfastly maintained the unity of the complement, but neither his experiments nor his conclusions seems confirmable.

Cytolysins. As might be expected from the effect of red blood cells, many animal cells can be shown to produce in the blood of inoculated animals substances which will destroy these cells, or cytolysins. In such a way spermotoxin (or spermolysin) was produced by Metchnikoff, epitheliolysin by von Dungern, nephrolysin by Lindeman, and leucocytolysin by Metchnikoff. And in analogy with the hæmolysins the various cytolysins can produce antibodies such as antispermotoxin, etc. The exact parallelism of construction and formation of such bodies with the hæmolysins, according to Ehrlich's theory, need only be indicated. Whether isocytolysins can be formed is as yet problematical.

Agglutinins and Precipitins. The phenomena of hæmolysis and bacteriolysis are usually accompanied by the presence of a marked agglutination of the bacteria or the red blood-corpuscles as the case may be. But such coagulative phenomena are entirely independent of any destructive property in the serum, as is shown by the fact that perfect bacteriolysis or hæmolysis may occur without any agglutination, and the well-known fact that red blood-corpuscles are agglutinated by practically any normal sera which, however, may possess no hæmolytic power. Agglutination, then, is simply a parallel phenomena in the course of immunization, and, according to Walker, in the case of bacteria, parallel with the antimicrobic rather than with the actually protective power of the serum. That agglutination will assist bacteriolysis and hæmolysis is quite probable. The exact mechanism of the process is unknown; Grüber has regarded it as due to some deleterious effect on the membrane of the bacteria which makes them sticky, while others have explained it on a chemical basis, inasmuch as similar effects may be produced by very dilute chemical substances, such as chrysoidin.

In 1897 Krause showed that antitoxins frequently gave a precipitate when mixed with their own toxins, but never with other toxins. Bordet then showed that absolutely specific precipitating bodies could be produced by inoculating rabbits with the milk of various animals. Meyers and also Uhlenhuth have found precipitins for peptones, and also for various kinds of egg albumin, the latter, however, not being absolutely specific, owing, doubtless, to the similarity of constituents in certain of the albumins employed. Bordet in his first observations on hæmolysis noted also the concurrence of a precipitate. Wasserman and Schütze, in 1900, found that this precipitate was specific, for rabbits when inoculated with various bloods gave sera which precipitated only the blood used. In the case of human blood the observations of these authors, together with those of Nuttall, make it probable that we have here a sure method of differentiating human blood and blood stains from the blood of other animals, excepting that of the monkey.

According to the Ehrlich hypothesis agglutinins and precipitins are uniceptors, composed of a haptophore group and a "coagulative complex."

Apart from its theoretical interest, this concept of Ehrlich as we have outlined it is of twofold value: it gives us a rational basis for serum therapy as we have it, and suggests by analogy the problems of the serum therapy that may arise.

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REVIEWS.

UTERINE TUMORS, THEIR PATHOLOGY AND TREATMENT. By W. ROGER WILLIAMS, Fellow of the Royal College of Surgeons. London, Paris and Madrid: Baillière, Tindall & Cox, 1901.

THIS book, which is quite up to the high standard of the author's previous works, is perhaps the best monograph on the subject which has yet appeared. It is truly a philosophical treatise, and the object has been the generalization and reduction into order of the masses of chaotic facts which may be found scattered through medical literature on the subjects of the pathology and treatment of uterine tumors.

The origin of uterine tumors is shown to be more closely associated with embryology and the aberrant elements, or so-called "rests," than with bacteriology; at the same time, the complications which arise as a result of bacterial influences are admitted. Uterine fibroids are properly termed "myomata," and there are several excellent chapters on their pathogenesis, morphology, biology, and complications.

The question as to whether benign tumors are peculiarly apt to become malignant is settled in the negative, and while it is admitted that myomata and malignant disease are sometimes concomitant in the uterus, it is pointed out that in such cases the two neoplasms are generally quite separate and independent, and that myomata are far less liable to originate cancer than are the glandular elements and embryonic remnants or "rests" in the uterus itself.

The chapters on the operative treatment of myomata and cancer are clear and reflect the best teaching of the day. Preference is given to the abdominal route, whenever practicable, in both classes of cases. The extra-peritoneal treatment of the cervical stump in the abdominal wound after supravaginal amputation is admitted to be obsolescent if not yet obsolete in conservative England.

Hysteromyomectomy with intra- or rather subperitoneal treatment of the stump, which should always be associated with the name of Bear, is credited to Schroeder, and in the chapter on the operative treatment of cancer no mention is made of combined vaginal and abdominal hysterectomy, an operation which is of distinct advantage in many cases.

The chapters on morphology and the general pathology of uterine cancer are most interesting and instructive. The author in 160 personal consecutive cases of cancer of the uterus found only 4 of the corpus, or 1 in 40; but he points out that these cases were not specially selected for their operative suitability. He believes that 90 per cent. of all uterine cancers are of the cylinder-celled (mucosal or glandular) variety, which he says should be regarded as the typical form for this organ. He points out that in this conclusion he differs from Cullen, who out of 141 cancers of the lower part of the uterus found that 123 were of the squamous and only 18 of the glandular type, and he says

that such a result could only be arrived at by interpreting the histological appearances differently to what he has done, and he believes that Cullen's interpretation is erroneous. The book contains 58 engravings which fairly well illustrate the text. J. B. S.

THE PRINCIPLES OF PATHOLOGICAL HISTOLOGY. By HARVEY R. GAYLORD, M.D., Professor of Surgical Pathology in the University of Buffalo, etc., and LUDWIG ASCHOFF, M.D., Professor and First Assistant in the Pathological Institute of the University of Göttingen. With an Introductory Note, by WILLIAM H. WELCH, M.D., Professor of Pathology in the Johns Hopkins University. Illustrated with 81 engravings in the text and 40 full-page plates. Philadelphia and New York: Lea Brothers & Co.

THE plan of this work is substantially that of a laboratory guide. In the first chapter we find directions for the preparation and examination of tissue, both fresh and hardened. The methods given are well selected, and include practically all of the important special stains now in use, as well as the standard stains generally used in laboratories. The directions are clear and full. The second and largest part is devoted to special pathological anatomy, the classification being based on organs, including the mucous membranes and the serous membranes—with tumors and blood. The laboratory idea is still further suggested by summaries of normal histology preceding the descriptions of the alterations of each organ. The work does not, therefore, aim at a complete exposition of morbid histology, yet the authors have included a wide range, and the reader can usually find information on any point, while the descriptions are admirably clear and detailed. The plan followed involves the further risk of not impressing the student sufficiently with the principles of general pathological anatomy, a risk that has not been so successfully avoided, as in the case of tubercle. In this part of the book we find its chief novelty, perhaps even its *raison d'être*, in the numerous heliotype reproductions of photomicrographs. With very rare exceptions these are admirably chosen and perfectly reproduced, and form a noteworthy addition to medical illustration. They compare favorably with the more costly reproductions that have been used in special works, and show the practical possibility of something far better than the half-tones now so much used. Very few of the illustrations are actually poor, but the one showing typhoid bacilli with flagella cannot be otherwise described, and the other photographs of bacilli in the same plate do not exceed mediocrity. As a rule, the amplifications are well adapted, but the important picture of miliary tuberculosis of the lung (Fig. 4, Plate XIII.) might well have been more highly magnified. It would have been more satisfactory if the amplifications had been expressed in diameters rather than in general terms, as high, low, etc. Although such works as this have a very important place, they do not give one a belief in the absolute superiority of photographs over good drawings as aids to the study of histology. We think we have noticed a greater tendency to neglect the art of focusing among students who use text-books with photomicrographic illustrations. A single plane

or even a foggy preparation often seems satisfactory to them. For special purposes, however, and with proper instruction, the newer method has a most important place. The illustrations in the text in the present work are, as a rule, good. Fig. 18, however, does not show much. The tricolor photographs will be examined with great interest, and those who are not aware of the progress of this art will be surprised at their excellence. But a comparison with the lithographs will show, as might be expected, that the former are not yet able to replace drawings, and are far from sufficing to settle doubt as to the nature or even the existence of newly discovered histological elements. The short section on Blood, by Dr. Irving Phillips Lyon, is very satisfactory as far as it goes. The addition of a chapter on the Principles of Optics and Photomicrography, with a brief account of reproduction processes, is a most happy one, and makes still more desirable this valuable and timely work. The only serious fault we have found is the very incomplete index, but this, and some typographical errors, can easily be remedied. Mechanically, the execution of the book is most satisfactory, and the cost is relatively so moderate as to ensure the wide use the work deserves.

G. D.

HANDBOOK ON SANITATION: A Manual of Theoretical and Practical Sanitation for Health, Sanitary, Tenement-house, Plumbing, Factory, Food, and other Inspectors, as well as for Candidates for all Municipal Sanitary Positions. By GEORGE M. PRICE, M.D., Medical Sanitary Inspector, etc. New York: John Wiley & Sons, 1901.

THE author states in his preface that he has been induced to undertake the work by reason of the "very few sources where the necessary knowledge of sanitation can be gained by those who propose undertaking sanitary inspection as a livelihood," and expresses the hope that he has presented the subject in such form that the student and candidate may make a creditable showing in the civil-service competitive examinations and obtain the desired position. He says truly: "The first step in the study of sanitation is to understand the principles of the science," and then proceeds to demonstrate with unusual clearness that his posing as a teacher is an admirable example of the blind leading the blind. Perusal of the book by one having even a superficial knowledge of hygiene can hardly fail to excite wonder that so much misinformation and nonsense can have been compressed into so small a space without entangling a larger measure of fact. Though doubtless well intentioned, the work is undeserving of serious notice except in so far as it is important to warn against all such short cuts to scientific knowledge, which are capable of doing much injury. A critical review of the very numerous chapters—most of them, fortunately, very brief—would require more space than can ordinarily be accorded a work of the highest excellence, and a few examples will, therefore, have to serve as an index of the general worthlessness of the entire work.

We are informed that "pathogenic bacteria are either those formed during the progress of organic decay . . . or those which become lodged in the soil through the contamination of the latter by groundwater and air, and which find in the soil a favorable culture medium

until forced out of the soil by the movements of the ground-water and air." We learn that "the peculiar disease called cretinism, as well as goitre, has been traced directly to a certain chemical composition of the soil," and must regret that he who holds this secret should fail to reveal it in more explicit terms. Contrary to what is now generally accepted, it appears that malaria and other paroxysmal fevers, tuberculosis, rheumatism, neuralgia, etc., are directly due to high-water level and marshy ground. Among the diseases due to soil influences are cholera, plague, yellow fever, and septicæmia. Under "Air," we learn that the greatest amount of carbonic acid "in confined spaces after the air has been breathed by people" is 6 parts in 10,000, and that "the carbonic acid content of air is taken as the standard of impurity," when we have supposed it to be an index of the amount of contamination. Bacteria appears in one place to constitute a kingdom by themselves and in another to be a part of the animal kingdom. Thus, "the impurities in the air according to their substance and character are as follows: mineral, vegetable, animal, bacteria, and gases," and among the animal particles found in air the author includes "the various micro-organisms" Carbonic acid in large amounts is said to be a "violent poison."

Although it may be true that "we may truthfully say that there is hardly a disease which is not directly or indirectly caused by the impurities found in the air," we have as yet no very direct evidence that such diseases as chronic interstitial nephritis, locomotor ataxia, cirrhosis of the liver, gonorrhœa, and syphilis are air-borne, nor can we reconcile the statement with the author's assertion that goitre, rheumatism, malaria, tuberculosis, neuralgia, cholera, plague, yellow fever, and septicæmia are due to soil influences.

Under "Ventilation," we learn that, "as a rule, the height of a room ought to be about one-third of the cubic space," and since the air space needed is said to be 1000 cubic feet, we are led to infer that the height of the room should be "about one-third," or 333⅓ cubic feet. Perhaps he means the cube root. The three forces mentioned as the active agents of ventilation are "diffusion, motion, and gravity."

Under "Water Supply," it appears that artesian wells are those over fifty feet in depth; that boric acid is one of the chemical agents used in the purification of water; and that Ancus Martius began the first Roman aqueduct two years after the generally accepted date of his death.

Nobody will question the statement that "the amount of refuse and garbage in cities is quite considerable," but not all will admit that the chief constituents of sewage include potash and phosphoric acid. If "sewer gas" is present in a room a piece of unglazed paper, saturated with a solution of acetate of lead and hung therein, "will be immediately blackened," but, we may add, not unless there is also present in full operation some form of sulphuretted hydrogen generator.

It appears that milk contains 12.83 per cent. of solids, divided as follows: fat, 3.69; carbohydrates, 4.88; salts, 6.71; total, 15.28—and no proteids. The salts have been supposed hitherto to amount to about 0.70, and milk has been noted as a valuable proteid food. Chalk is mentioned as an adulterant of milk, although never found. The lactometer is mentioned as a valuable assistant in milk inspection, and the instrument is shown in an illustration. Whatever the instrument from

which the drawing was made may be, it certainly is not a lactometer, and cannot be used as such. It appears to be a portion of a complicated piece of chemical apparatus, whereas a lactometer is exceedingly simple in construction.

As a whole, while the book may not cause the unskilful to laugh, these not being able to note its grotesqueness, it certainly is calculated to make the judicious grieve. C. H.

ATLAS AND PRINCIPLES OF BACTERIOLOGY. By PROFESSOR DR. K. B. LEHMANN and R. O. NEUMANN, Drs. of Philosophy and Medicine. Edited by GEORGE H. WEAVER, M.D. In two Parts. Philadelphia and London: W. B. Saunders & Co., 1901.

LEHMANN and NEUMANN'S work is now well known and its value established. It is an excellent work; with certain limitations it covers the field satisfactorily, and the illustrations in the Atlas leave little to be desired. We believe that accurate drawings for the purpose of studying bacteria are more valuable than photographs. This is particularly true in the representation of cultures, a fact to which Lehmann calls especial attention in his preface. There is some question whether the plan adopted here of representing all cultures upon a black background is entirely satisfactory. The greatest virtue of any drawing is the accurate representation of nature, and any form of diagram is a poor substitute unless the actual picture is so complex that its essential details cannot be appreciated by the uneducated eye. It is possible that the mechanical difficulties in the reproduction of the cloudy amber-color of the agar culture media, or the transparency of the gelatin culture media was so great that the present method was on the whole better. As far as it goes it is exceedingly satisfactory, and perhaps, for purposes of diagnosis, it is all that could be demanded. Practically all the important organisms are represented, and in such a variety of forms and cultures that any other Atlas would rarely be needed in the ordinary hospital laboratory.

The most interesting part of such a work is of course the general section; the most useful, the special section. Lehmann's article on the general aspects of bacteriology is one of the most satisfactory that we have ever read. It is thorough, approximates completion sufficiently; it is clear, and devotes itself rather to facts than to theories. The discussion of immunity is perhaps somewhat briefer and less thorough than the other parts of the book. The subject of agglutination receives such scant consideration that it might well have been omitted. Widal, who has certainly done more to promote the utility of this reaction in typhoid fever than any other man, is barely mentioned, and then only in connection with one of his subsidiary suggestions. In the article upon the typhoid bacillus the statements on this subject, in view of its extreme importance, are even less adequate than in the general section. In the discussion of the classification Lehmann is at his best. He places it upon a clear scientific basis, recognizes the difficulties, suggests methods for overcoming them, and, as far as possible, urges the great importance of a thorough study of the individual species of bacteria.

While not advocating names etymologically incorrect, he does not believe in changing those already suggested, because, after all, the important thing is to designate the genera and species and not to avoid hybrids of Greek and Latin. The classification which he adopts is based upon rational principles, and, as a matter of fact, is one of the most satisfactory at present in use. The subdivision of the family bacteriaceæ into the bacterium without endogenous spores and bacillus with endogenous spores will be difficult to carry against the habit of the world of calling all rod-shaped organisms bacilli. We agree with Lehmann that any practical division into the pathogenic and non-pathogenic bacteria is absurd. There is no scientific distinction between the pathogenic and non-pathogenic excepting in regard to their action upon certain living organisms, and it is not impossible that there are few species that are not pathogenic for some form of life. On the other hand, there is accumulating evidence that the so-called pathogenic and non-pathogenic bacteria may pass one into the other. The descriptions of the individual species are concise, clear, and thorough; the translation is fair. There is a distinct flavor of the original German, such as complicated adjectival phrases and a persistent use of the inverted sentence. We think that in another edition the book might be improved in this respect, and yet it must be admitted that the language is quite comprehensible, although we doubt whether it would be so to a reader not familiar with the German language. J. S.

CARE AND TREATMENT OF EPILEPTICS. By WILLIAM PRYOR LETCHWORTH, LL.D. New York and London: G. P. Putnam's Sons, 1900.

THIS work is not medical in the narrow sense of the word. It does not tell what physic to give epileptics. It is a careful study of the question of what the State and charitable persons owe to the epileptic as an unfortunate who, not being able to care for himself, must be guarded and cared for. It is a very careful study of a serious social problem. The author gives an account of what measures have been taken in the several States and in foreign countries to aid epileptics by institutional treatment. It is to the discredit of America that the problem has been more successfully treated in several European countries than by us. Indeed, the first attempts began abroad, and have only been slowly followed here. No class appeals more worthily for aid, and yet, as compared with the insane and feeble-minded, they have been sadly neglected. Every State should have an institution in the country—a large farm, not a mere house of detention—where patients could live a hygienic life, work out-of-doors, and have rational and healthy amusements. Apart from the moral duty we owe to unfortunates as a business question, it probably would be cheaper to properly care for epileptics than to neglect them. Prisons and houses of correction, institutions which cost money to support, contain not a few epileptics who pass in and out repeatedly, or, finally, get themselves hanged, which also costs money. It might be cheaper to prevent crime by proper care. How much has been done and how much more remains to be done this excellent book well shows. C. W. B.

DIFFERENTIAL DIAGNOSIS OF THE SEPARATE FORMS OF GALLSTONE DISEASE. By PROF. HANS KEHR (Halberstadt). Authorized translation by WILLIAM WOTKYNS SEYMOUR, A.B. Yale, M.D. Harvard. With an introduction by Prof. Kehr. 12mo. Pp. 370. Philadelphia: P. Blakiston's Son & Co., 1901.

PROF. KEHR divides this very excellent book into two parts, Part I. consisting of four lectures on the pathology, the examination, the special diagnosis, and the treatment of cholelithiasis, while Part II. gives the clinical and operative histories of one hundred cases, illustrating the various conditions and difficulties which the disease may present. In addition there is an appendix containing the histories of eighteen more operative cases, with remarks on inflammatory jaundice, and insidious infection of the biliary system.

In the introduction Kehr states that he has operated 547 times for gallstones, and his remarks and conclusion on the diagnosis and treatment of cholelithiasis are based on this enormous and unprecedented experience. It would, therefore, be idle for us to criticise his opinions on diagnosis or operative technique, for the experience of surgeons in this country is limited to dozens of cases, where he deals in the hundreds. In his opening lecture he takes the ground that few clinicians have had the experience to make an exact diagnosis in cholelithiasis, for the reasons that the experience of the majority is limited to cases subjected to medical treatment or those that come to the post-mortem table. The book, therefore, is intended primarily to assist the general practitioner in making an exact diagnosis, and detailing to him the brilliant possibilities which surgical treatment holds out.

Kehr states that the symptoms of gallstone disease arise almost invariably as the result of inflammation and infection; in other words, that gallstones may remain an indefinite time in the gall-bladder without occasioning a symptom until a trauma or infection occurs. The pain experienced, he explains, is due either to the swelling of the gall-bladder and ducts or to adhesions binding these tracts to neighboring organs. That pain is excited by the mere presence of the stone, he considers most unlikely and very exceptional, even when the stone is lodged in the common duct. He also states that the majority of the pains which are called cramps of the stomach, occurring in adults, are of gallstone origin.

Under the heading of special diagnosis, the subject-matter is extremely good and rich in ideas, but the arrangement of it is possibly not as systematic as it might be. A concise table in this chapter gives twelve different forms of the disease with their prominent differential symptoms, and their appropriate treatment.

The chapter on treatment represents the best modern views. He does not advocate operation in every case where gallstone is diagnosed, believing that many mild cases can be relieved under appropriate medical treatment. At the same time he gives a clear picture of the results of prolonged medical treatment in cases where the knife should have been used. He, therefore, takes the middle ground between von Winniwater and Kraus, the former believing that the diagnosis of gallstone should indicate operation, and the latter that surgical intervention should be sought only upon a vital indication. He sums up the action of the Carlsbad treatment with Sprüdel water in a few words: It

allays the inflammation of the biliary passages and renders the disease latent, freeing the patient from pain, but has no power to dissolve or remove the stone. In other words, its action is like a hot poultice or opium.

His operative statistics are interesting. When the gallstones are only found in the gall-bladder his mortality has not yet exceeded 1 per cent. Where it is necessary to excise the gall-bladder the mortality reaches 3 per cent., but when the common duct has to be incised it rises to 10 per cent. The troubles which sometimes develop after successful operation he ascribes usually to adhesions, the fixation of the gall-bladder to the abdominal wall, etc., and not to stones left behind or again developing. Many points in his operative technique will appeal to the surgeon. His strong objections to exploratory puncture of the gall-bladder or massage of that organ when distended are well taken, and he places such procedures under the heading of technical sins.

Dr. Seymour has accomplished a good work for the profession in reproducing in English the experiences of so eminent an authority, and he is to be congratulated upon the literalness of the translation.

R. G. LE C.

THE PRINCIPLES OF HYGIENE: A Practical Manual for Students, Physicians, and Health Officers. By D. H. BERGEY, A.M., M.D., First Assistant, Laboratory of Hygiene, University of Pennsylvania. Octavo volume of 495 pages, illustrated. Philadelphia and London: W. B. Saunders & Co., 1901.

THIS very excellent and valuable book presents in compact form a very clear exposition of the general principles of hygiene. The author disclaims in his preface any attempt to treat the subject exhaustively, his object being "to give the general principles upon which the health officer and the physician work in their respective capacities in dealing with conditions which are detrimental to health or which tend to improve it."

The subjects considered include air, ventilation, heating, water and water-supply, removal and disposal of sewage, garbage disposal, food and dieting, soil, habitations, vital causes of disease, disinfection, quarantine, vital statistics, exercise, clothing, and military, naval, personal, industrial, and school hygiene, all of which are presented clearly, concisely, and attractively. Especially to be commended is the chapter on vital causes of disease, the consideration of immunity and susceptibility being handled with signal ability and the whole subject presented in better form than, in the opinion of the reviewer, ever before in a work of similar character.

The book is faulty in some minor respects, such, for instance, as including with implied approval the arbitrary standards of purity of drinking-waters, which have long since been abandoned as unscientific and untrustworthy; but, as a whole, it commends itself for simplicity and accuracy. The appendix, containing rules for interchange of different expressions of results obtained in analyses, for conversion of thermometric degrees, etc., is, however, singularly unfortunate, since wrong

factors are given for converting nitrogen to nitrous acid and nitric anhydride, the rules for converting thermometric degrees of one scale into those of another are wholly wrong, and the United States gallon has been confused with the imperial gallon, which measure is not used in this country. C. H.

HAND ATLAS OF HUMAN ANATOMY. By WERNER SPALTEHOLZ, with the advice of WILHELM HIS. Translated from the third German edition by LEWELLYS F. BARKER, with a preface by FRANKLIN P. MALL. Vol. I., Bones, Joints, Ligaments. Leipzig: S. Hirzel. New York: G. E. Stechert, 1900.

THE German edition of this most excellent text-book has long been familiar to students of anatomy, and it is the experience of its practical value that has led the well-known teachers of anatomy, whose names figure upon the title-page, to further its publication in English. The special feature of the book is to be found in the illustrating. As in most German text-books of anatomy, the text plays a subordinate part, and the student is taught the appearance of the anatomical structures by his sense of sight and not by his ability to memorize anatomical terms. The plates are most accurate and have been executed with the greatest care, the illustrations of the present volume being reproduced from the original plates. It is doubtful whether any book on anatomy can ever altogether supplant his Gray in the heart of the American medical student of the present generation, but Spalteholz, without supplanting the other book, will make a useful companion to it. J. H. G.

THE MEDICAL NEWS POCKET FORMULARY. By E. QUIN THORNTON, M.D., Demonstrator of Therapeutics, Pharmacy, and Materia Medica in the Jefferson Medical College. Philadelphia: Lea Brothers & Co.

IN the preface to his first edition the author says that "no man of independent thought will be hindered in his development by having the best information placed conveniently at hand."

That the medical profession agrees with the above statement of the author is shown by the publication of the fourth edition of the book.

The little volume contains besides the large collection of formulæ a comparative table of the metric system, a list of the important incompatibles, a synopsis of the treatment of poisoning by the various drugs, and a complete table of the doses of the drugs of the Pharmacopœia expressed in the metric system as well as in the usual apothecaries' method. Due space is also given in the collection of formulæ to the more recent preparations. One of the most important points to the physician after he has made up his mind as to the proper drug to order in any case is how best to exhibit it, and the author has expended great care as to the palatability and pharmaceutical elegance of the preparations without, however, sacrificing therapeutic efficacy. W. R. N.

INTERNATIONAL CLINICS. Edited by HENRY W. CATTELL, A.M., M.D., Philadelphia, with the Collaboration of Various Authors. Eleventh series. Vol. III., pp. 303; Vol. IV., pp. 302. Philadelphia: J. B. Lippincott Co., 1901–1902.

IN the six hundred pages of these two volumes we find many articles of great practical, and some of permanent, value. The subjects are ample in range and in the main well presented. Clinical Aspects of Spa Treatment, by Robinson; Localization of Nervous Diseases, by Wiener; Clinical Laboratory in Private Practice and in the Physician's Office, by Camac; and Some Results of Microbic Infection in Urinary Disease, by Heming, are of marked interest. Winged Insects and their Larvæ as Parasites of Man, by Walsh, is both readable and instructive, as is his other paper on Prophylaxis and Early Diagnosis in Heart Disease; Palpitation and Organic Disease; Tobacco and Heart Lesions; Cure of Heart Lesions. Broca's plea for Small, Repeated Doses of Solutions of Mercurial Salts in treating Syphilis, Guinard's Modified Technique in the Spinal Injections of Cocaine, and Jonnesco's Splenectomy for Malarial Cachexia, are important contributions, the last two suggestive. Burnett points out the dangers of too strong solution of adrenalin chloride, and Taylor illustrates Deformities in Children from the stand-point of the General Practitioner. This article is doubly interesting from its graphic descriptions and because it not only demonstrates that the general practitioner exists, but, as well, that he is observant and practical. We wish that Newton had treated pulmonary osteo-arthropathy more fully, although his carefully reported case is a real addition to the somewhat meagre literature. We have on other occasions spoken favorably of this series, and we have criticised when on one occasion a volume did not meet our expectations. Of those under consideration we believe that a full measure of value is given, and the various authors have ably seconded the editor in his efforts to make *International Clinics* represent the present status of the healing art. R. W. W.

GYNECOLOGICAL PATHOLOGY: A MANUAL OF MICROSCOPIC TECHNIQUE AND DIAGNOSIS IN GYNECOLOGICAL PRACTICE, FOR STUDENTS AND PHYSICIANS. By Dr. CARL ABEL, Privat-Docent, Berlin; translated and edited by SAMUEL WYLLIS BANDLER, M.D, Adjunct Gynecologist to Beth-Israel Hospital, New York, with a chapter on the Embryology of the Female Genitalia and the Pathological Growths Developing from Embryonal Structures. Illustrated by one hundred engravings. New York: William Wood & Co., 1901.

THIS translation brings within the reach of the English student a book which was perhaps the first on the subject in any language, and which immediately took its place as a standard work in the comparatively new field of gynecological pathology. The translator has added an excellent chapter on embryology and on the origin of growths from embryonal cells and organs.

Part I. contains 21 pages, and deals with the technique of obtaining and handling the material for examination. The directions are concise and are the result of a large experience. The few illustrations in this part are unnecessary.

Part II., of 143 pages, is on diagnosis, and deals with the macroscopical and microscopical appearances of the various pathological conditions of the vulva, the vagina, the cervix uteri, the uterus, the tubes, and the ovaries. Special attention is directed to microscopical illusions, and the student is warned to be on his guard, especially in making the diagnosis of carcinoma of the cervix. Before considering the pathology the normal anatomy of each structure is given. There is an excellent chapter on the normal anatomy of the uterus during menstruation, during the first months of intra-uterine pregnancy, and in extra-uterine pregnancy.

Part III., 59 pages, has been added by the translator, and deals with the embryology of the female genitalia and the pathological growths developing from the embryonal structures. The subject is made unusually clear, and the illustrations are selected from such well-known authorities as Waldeyer, Keibel, Kollman, His, Lemon, Schultze, and Nagel.

The book is intended to serve as an introduction to practical experience in gynecology, and is the result of a large clinical experience. The value of the book would be greatly increased by more liberal illustrations of the various microscopical appearances described.

J. B. S.

TEXT-BOOK OF PHYSIOLOGY. Edited by E. A. SCHAFER, Professor of Physiology, University of Edinburgh. Vol. II. Edinburgh and London: Young J. Pentland. New York: The Macmillan Co., 1900.

THE first volume of Schäfer's *Physiology* appeared several years ago, and it is pleasing to observe that the second volume of this encyclopedic work is fully as interesting and valuable as the first. The authors of the various articles in this volume are: Leonard Hill, W. H. Gaskell, J. B. Haycraft, E. H. Starling, J. Burdon Sanderson, Francis Gotch, E. A. Schäfer, J. N. Langley, C. S. Sherrington, W. H. R. Rivers, John G. McKendrick, and Albert A. Gray, all of whom may be regarded as authorities on the various matters of which they treat. The contents of the volume include many interesting articles on the various portions of the circulation and the nervous system, and the sections on the organs of special sense; the latter are particularly to be commended as possessing great value to the general practitioner or specialist who desires to look up some physiological data in regard to the senses of vision, hearing, or smell.

The book may be regarded as probably the most complete exposition in English of modern physiological research. It does not wholly answer to our idea of a text-book, as it more corresponds to a system than to a book for use by students. It makes a bulky volume, but when the value of its contents is considered one is glad that no attempt was made to condense the subject-matter.

G. M. C.

MEDICO-SURGICAL ASPECTS OF THE SPANISH-AMERICAN WAR. By LIEUTENANT-COLONEL DR. NICHOLAS SENN, Chief Surgeon U. S. V.; Chief of Operating Staff with the Army in the Field; Professorial Lecturer on Military Surgery, Chicago University. Chicago: American Medical Association Press, 1900.

THIS book is largely a reproduction of a number of articles which have appeared from the pen of its eminent author. Where subjects of practical surgical importance are under consideration, its contents are most interesting. The descriptions of the organization of various branches of the hospital service in a large army should be read by all who are interested in the subject, containing as they do much practical advice drawn from the author's personal experiences. Camp hygiene is fully entered into. The proper location and construction of sinks, the various sources proper to be utilized for water-supply, and the practical care of the men is gone into in detail. Particularly interesting are Dr. Senn's descriptions of various cases which came into his hands for operation and treatment. The Spanish-American war offered an excellent opportunity for the study of wounds produced by modern small arm projectiles, and Dr. Senn utilized that opportunity to its fullest extent.

The book, however, has certain very obvious defects. It contains many irrelevant and poorly executed illustrations, such as portraits of President McKinley and General Shafter; of Miss Wheeler attired as a hospital nurse, and of groups of hospital stewards and medical officers of the Illinois National Guard, and a portrait of the wife of the Governor of the State. It bears evidence also of hasty composition. As over two years have elapsed since the termination of the war, it certainly seems a pity that the distinguished author did not see fit to revise and edit his manuscript and eliminate much useless material for the sake of that which was of value.

The typography of the book is lamentably deficient. A number of pages could be picked out in which lines are entirely separated from their context, thus, on page 12, there stands as a lonely sentence, "There was probably never a day when their duty." No explanation can be found anywhere throughout the book as to what this sentence refers to.

F. R. P.

THE PATHOLOGY AND SURGICAL TREATMENT OF TUMORS. By N. SENN, M.D., Ph.D., LL.D. Second edition; revised. Philadelphia and London: W. B. Saunders & Co.

RECENT work done in Rome upon the parasitic origin of malignant tumors has been added to this volume. A new section has been added upon sarcoma of the decidua.

This work of Professor Senn is most comprehensive and exhaustive in its scope. After considering general questions of the origin, morphology, anatomy, and pathology of tumors, tumors of plants and animals are described. Then the clinical appearances in general, the diagnosis, prognosis, and treatment in general are considered.

The succeeding chapters describe each variety of new growth sepa-

rately as it occurs in the different tissues and organs of the body of the human individual. For example, under adenoma is the heading mammary gland, and under this heading will be found all that is of value concerning adenoma of the mammary gland, so that the book is a splendidly arranged reference-book upon tumors.

The importance of careful teaching in the diagnosis of tumors can hardly be overestimated. In few medical schools is the diagnosis of tumors taught systematically and with proper clinical material. The chapter upon the diagnosis of tumors, p. 88, is full of suggestions to the teacher of clinical surgery. The sense of sight and touch should be exercised to their full extent before additional assistance is sought in aspirators and harpoons, etc. The physical conditions of the growth are very important in determining its nature. Operative procedures requiring especial manipulations are described in connection with the organ involved. That the teaching of the diagnosis of tumors should be taught as a special branch in our medical schools is coming gradually to be recognized. This book of Dr. Senn's very admirably emphasizes the importance of this branch of surgical pathology. The number of original and new illustrations is commendable. C. L. S.

THE AMERICAN YEAR-BOOK OF MEDICINE AND SURGERY FOR 1902. A yearly Digest of Scientific Progress and Authoritative Opinion in all branches of Medicine and Surgery, drawn from journals, monographs, and text-books of the leading American and foreign authors and investigators. Arranged, with critical editorial comments, by eminent American specialists, under the editorial charge of GEORGE M. GOULD, A.M., M.D. In two volumes: Vol. I., including General Medicine, octavo, 700 pages, illustrated; Vol. II., General Surgery, octavo, 684 pages, illustrated. Philadelphia and London: W. B. Saunders & Co., 1902.

UP to the present date no better substitute for the much to be lamented *Index Medicus* than the form of publication known as the year-book has presented itself. There are many varieties of publication which aim to present in compact form the gist of the most valuable contributions to medical literature; thus most of the medical journals have an abstract department, aiming thereby to present to their readers an epitome of current literature as it appears; but this can never be so satisfactory a method as that which combines in book form and under classified headings the same kind of material.

The American Year-Book is issued in two volumes: one entitled "General Medicine," the other "General Surgery." These volumes are sold separately, and thereby enable the purchaser to procure the one which contains those subjects in which he is especially interested. It is impossible to attempt an analytical review of such a *mêlange* of riches as each volume presents. The contributions to them are not merely abstracts from literature, but they constitute critical essays by competent authorities on the different subjects considered.

The work is a standard, and its possessor may congratulate himself upon having on his book-shelves the sum and substance of all that is really worthy of preservation out of the vast mass of medical literature which has appeared during the past twelve months. F. R. P.

DISEASES OF THE NOSE AND THROAT. By D. BRADEN KYLE, M.D., Clinical Professor of Laryngology and Rhinology, Jefferson Medical College, Philadelphia; Consulting Laryngologist, Rhinologist, and Otologist to St. Agnes' Hospital. Second edition, revised. Octavo, 646 pages; over 150 illustrations and 6 lithographic plates. Philadelphia and London: W. B. Saunders & Co., 1901.

THE first edition of Dr. Kyle's book well merited the success which has brought about the publication of the second edition. The second edition has been carefully revised and several minor errors which appeared in the former have been corrected.

The grouping and classification of the various pathological conditions met with in the nose and throat is particularly to be commended. Some exception may be taken to the author's system of nomenclature, but Dr. Kyle is a trained pathologist and his definitions and studies are based upon thorough pathological research.

There is a notable absence of reference to foreign literature in rhinology, but it is well compensated by the large number of American authorities whose work in this specialty is acknowledged and referred to.

It may be regarded as one of the standard American text-books on the subject of rhinology. F. R. P.

THE RÖNTGEN RAYS IN MEDICINE AND SURGERY. By FRANCIS H. WILLIAMS, M.D. 8vo., pp. 639 and index. Fully illustrated. New York: The Macmillan Co., 1901.

IN discussing the application of this new method of diagnosis, Dr. Williams has followed the trend of his previous writings, and shows a decided preference for the development of technique in fluoroscopic examinations. He undoubtedly ranks among the first in the acquirement of an ability to see and interpret what he sees upon the fluorescent screen. He devotes the major part of this work to the description and discussion of his apparatus and methods and their result. This work is particularly valuable to those desirous of following his methods and of acquiring such technique and the ability to see and interpret the transient images seen with the fluoroscope.

The description of the static machine which he favors is given in detail, but too little space is devoted to the description of other forms of apparatus and other tubes than those he prefers to make the book "A Guide to Practitioners and Students" in this method of diagnosis. It should have dealt with the apparatus and technique of other investigators to a fuller extent if he desired it to be universal in its application. As it is, it is a guide to the technique and practice of the author, and as such is very valuable.

While discussing the application of this method in surgical diagnosis, it fails to give sufficient assistance to the student in detailing the technique and methods of making the skiagraphs which afford the basis of accurate and reliable diagnosis. C. L. L.

VENEREAL DISEASES: A MANUAL FOR STUDENTS AND PRACTITIONERS. By JAMES R. HAYDEN, M.D., Chief of Clinic and Instructor in Venereal and Genito-urinary Diseases at the College of Physicians and Surgeons, New York, etc. Third and revised edition. Philadelphia and New York: Lea Brothers & Co.

IT affords us considerable satisfaction to review a third edition of this little treatise, which we have for some time considered to be one of the best of all the manuals published upon the subject. It is a work eminently adapted to the needs of the medical student in particular, giving, as it does, in the words of the author, "in a clear and compact form, a practical working knowledge of gonorrhœa, stricture, chancroid, and syphilis." Several new sections have been added, and the whole volume has been sufficiently revised to bring it thoroughly up to date.

The fad known as the "Janet method" for the treatment of gonorrhœa receives unqualified condemnation at the hands of the author, who advises a well-known and rather old-time method of treatment, which he styles a "rational" treatment. The chapters devoted to stricture and syphilis give in a concise manner most of that which students and general practitioners need to know upon these subjects. Indeed, this little volume will prove of great value to all those members of the profession too busy or disinclined to study more pretentious works on venereal diseases.

H. M. C.

MANUAL OF PHYSICAL DIAGNOSIS. FOR THE USE OF STUDENTS AND PHYSICIANS. By JAMES TYSON, M.D., Professor of Medicine in the University of Pennsylvania and Physician to the University Hospital; Physician to the Philadelphia Hospital; Fellow of the College of Physicians of Philadelphia; Member of the Association of American Physicians, etc. Fourth edition, revised and enlarged. With colored and other illustrations. 18mo., 298 pages. Philadelphia: P. Blakiston's Son & Co., 1901.

WITH each succeeding edition the subject-matter of this well-known manual has been carefully scrutinized, revised, amplified, and amended as seemed necessary to secure completeness and that detail possible in a book of its size. In the fourth edition the statements are accurate and the entire subject of physical diagnosis is presented in a manner attractive to the student.

The value of the book is increased by short chapters containing brief directions for examining the blood and the gastric contents and for making a necropsy. As a whole the book is unsurpassed by any of its size.

A. O. J. K.

PROGRESS

OF

MEDICAL SCIENCE.

MEDICINE.

UNDER THE CHARGE OF

WILLIAM OSLER, M.D.,

PROFESSOR OF MEDICINE IN THE JOHNS HOPKINS UNIVERSITY, BALTIMORE, MARYLAND,

AND

W. S. THAYER, M.D.,

ASSOCIATE PROFESSOR OF MEDICINE IN THE JOHNS HOPKINS UNIVERSITY, BALTIMORE, MARYLAND.

On the Presence of the Bacillus of Eberth in the Blood and in the Rose-spots during Typhoid Fever.—COURMONT (*Journal de physiologie et de pathologie générale*, 1902, vol. iv., p. 155) has made careful studies of the blood in all cases of typhoid fever entering his wards during the year 1901, nine in number. The typhoid bacillus was found in the circulation in every instance, and in many cases it was found at several different times in the course of the disease, leading the author to the conclusion that it is present in the blood as a rule in typhoid fever. In no instance did he obtain other than pure cultures. The bacillus may appear at an early period, inasmuch as it was found in one case on the fifth day. In order to obtain these results it is necessary to use a considerable quantity of blood in a large quantity of bouillon. In fourteen instances in which several drops of blood were inoculated in about 20 c.c. of bouillon only three positive results were obtained. He is inclined to believe that one should employ 300 c.c. to 500 c.c. of bouillon, which should be inoculated straightway from the syringe and introduced immediately into the thermostat. The results are by no means as good when the blood has been allowed to clot before taking the culture.

In some instances at the end of twenty-four hours the bouillon may seem sterile, but on shaking it up thoroughly a growth usually follows. From 2 c.c. to 4 c.c. of blood should be used.

The virulence of the bacilli obtained was rather marked. Their agglutinability was almost invariably markedly inferior to that of bacilli which had been maintained for a long time in artificial cultures. They were, for instance, agglutinated commonly at a dilution of 1 : 50 by a serum which agglutinated laboratory bacilli at 1 : 200. These characteristics were retained by the second or third generations. After many generations, however, they became less agglutinable. The typhoid serum acts apparently in the same

manner upon its own bacilli as upon others. There is no special sensibility of the bacilli in any given case to the serum of that particular patient.

There appears to be no relation between the presence of the typhoid bacilli in the blood and the agglutinating power of the serum. In four of the nine cases the bacilli were obtained while the agglutinating power of the serum was absolutely *nil*. The author concludes: "A search for the bacillus of Eberth in the blood by the above-mentioned method should be undertaken to make an early diagnosis of typhoid fever in every instance in which the Widal sero-diagnosis is negative."

Yet more remarkable are the results reported by POLACCO and GEMELLI (*Centralbl. f. innere Medizin*, 1902, vol. xxiii., p. 121). These observers have made a series of cultures from the rose-spots in fifty typhoid patients during an epidemic lasting from July until November, 1901. They used the method of Neufeld with certain modifications. The most important points they believe to be the necessity of taking a little of the tissue as well as the blood from the rose-spot and to use fluid culture media. In obtaining the substance they used the "Vaccinostyle Maréchal." They took their cultures always from at least two spots. The method is so simple that it is practicable with even small children. Positive results were obtained in every case, in many instances before the Widal reaction had appeared.

[It will be interesting to see whether these surprising results will be confirmed by other observers. Cole, in Professor Osler's clinic, has been able to demonstrate the presence of typhoid bacilli in the circulating blood by methods very similar to those of Courmont in about 80 per cent. of the cases, not infrequently before the development of the Widal reaction or before the appearance of roseola. A simple and practical method of demonstrating the presence of typhoid bacilli in the circulation in the first week of the fever would be of inestimable clinical value.—W. S. T.]

Organo-therapy in the Treatment of the Fatty Stools of Pancreatic Disease.—SALOMON (*Berlin. klin. Wochenschrift*, 1902, vol. xxxix., p. 45). A few observers have already pointed out that in cases with fatty stools, in the absence of jaundice, due inferentially to pancreatic disease, the administration by the mouth of fresh pancreas has resulted in marked improvement. The more careful observations of von Noorden indicated that commercial preparations of pancreatin are without essential value, that only the fresh pancreas is of use. Weintraud also observed that while preparations of pancreatin were of some value in furthering the absorption of albuminoids, yet they helped but little toward the absorption of fat.

Salomon reports two extremely interesting cases. The first was that of a woman, aged fifty years, who consulted him in June, 1900, having suffered for over a year from occasional attacks of diarrhœa and sensations of unrest in the abdomen, with a loss of twenty pounds. The stools contained large quantities of fat. A slight degree of glycosuria was present, which disappeared on diminishing the carbohydrates. The patient was given a careful diet in which the exact amount of fat and nitrogen was estimated. After a period of preliminary observation fresh pancreas was administered. It was clearly demonstrated that this treatment greatly increased the absorption of both fats and albuminoids. The character of the stools entirely changed,

and the distressing symptoms disappeared. Later on pancreatin prepared by Hausfeld in St. Gallen was administered in Sahli's glutoid capsules without essential effect upon the absorption of fats, although, as in the case of Weintraud, the nitrogen absorption was appreciably helped. On the other hand, the administration of 0.25 pancreatin of the Rhenania-Aachen firm, five times a day, resulted in marked benefit, though somewhat less than in the case of treatment with the fresh gland. A new preparation by the Rhenania firm, a compound of pancreatin and 10 per cent. tannin, to which the name pankreon has been given, appears also to have good effect, while in that it is unattacked by the gastric juice, it need not be given in glutoid capsules. In a second case similar results were obtained.

In connection with these cases the author points out another very interesting observation. Recent works have shown that the acetone body in diabetes probably arises from fat. If this observation be true one might expect that in cases like the above the formation of acetone should go hand-in-hand with the greater absorption of fat. This proved to be true in Case II., where the quantity of acetone was materially increased by the administration of pankreon, which, as has been mentioned, increased greatly the absorption of fat.

Intestinal Perforation by Ascaris Lumbricoides.—Solieri (*La Riforma Medica*, 1902, vol. xviii., p. 280) reports a case of a man, aged sixty-seven years, who, in perfect health, was seized with sudden abdominal pain, followed by evidence of an acute peritonitis. Laparotomy was performed twenty-seven hours after the onset. The peritoneum was found to be full of pus, feces, and ascarides. In a loop of the small intestine not far from the cæcum and opposite the mesenteric insertion was a round perforation from which feces and ascarides escaped. This was excised and an artificial anus made. The patient died nine hours later.

On microscopical examination it was found that the perforation was not in a Peyer's patch. The mucosa was normal throughout its extent and everted at the point of the ulceration, so that at some points it almost came into contact with the serous membrane. The submucosa and the muscular coat are cleanly cut through, normal histologically, and buried under the mucosa. The subserous and the serous coats showed changes dependent upon the peritonitis. Cocci and bacilli were found in scanty numbers on the surface of the mucosa and the serous membrane. Micro-organisms were not abundant in the tract of the perforation, not accumulated in colonies or deep in the tissues. The absence of small-celled infiltration of the internal and middle coats, the absence of necrotic or hemorrhagic areas, of tubercles, of marked changes along the course of the tract of the perforation, and the normal condition of the vessels were sufficient to exclude typhoid, tuberculosis, or inflammatory perforation. The author, therefore, considers himself justified in assuming that the perforation did not occur through a diseased area, but was the result of an "act of violence," which was exercised during a period of time so short as not to give time for manifestations of reactive inflammatory processes on the part of the tissues. In addition to this, in a number of the sections there were found under the serous coat distinct sections of an ascaris. A similar observation of an ascaris in the tissues of the

intestine has been made by Stork. The few cases in literature in which perforations by ascarides have been reported are referred to. Inasmuch as many of these have been doubtful in nature, this instance, which would seem to be unquestionable, is of considerable interest.

The Value of Subcutaneous Gelatin Injections in Melæna Neonatorum.—HOLTSCHMIDT (*Münchener med. Wochenschrift*, 1902, vol. xlix., p. 13) reports five cases of melæna neonatorum occurring in the gynecological clinic at Dresden during the year 1901, in which subcutaneous injections of a 2 per cent. solution of gelatin were used. During the seven years from 1894 to 1900 seven of the fourteen cases of melæna occurring in this clinic resulted fatally. All of the five cases occurring in 1901 recovered. As a rule, 15 c.c. of gelatin solution were used, and in two instances only was this repeated. While four of the cases positively recovered, one child left the hospital on the ninth day in a very serious condition, although there had been no hemorrhage for five days.

Early Syphilitic Hydrarthrosis.—DE GRANDMAISON and BOIDIN (*Archives Générales de Médecine*, 1902, p. 58) report an interesting case of acute hydrarthrosis of the left knee-joint in connection with secondary syphilis. This appeared simultaneously with the roseola, headache, dysphagia, and loss of hair, four weeks after the appearance of the initial lesion, and two months later, with a relapse after insufficient treatment, it returned a second time, entirely disappearing under satisfactory treatment on each occasion. The fluid from the knee-joint, which was of a lemon-yellow color, showed in the centrifugalized sediment, leucocytes and red corpuscles in the relative proportion of 70 and 30 per cent. These leucocytes showed lymphocytes, 73 per cent.; mononuclears, 11 per cent.; polymorphonuclears, 16 per cent. Ten cm. of the fluid were injected into a guinea-pig without result.

Literature contains so few cases of this nature that the authors deem it worthy of publication, and conclude that when one meets with joint swelling during secondary syphilis he should consider it in all probability luetic in nature, and that by the adoption of this treatment:

"1. He will cure his patient as far as the manifestations of syphilis may be cured.

"2. He will have occasion to control the exactness of his diagnosis in virtue of the old adage, *naturam morborum ostendunt curationes*."

On the Pathogenic Importance of Balantidium Coli.—HENSCHEN (*Arch. f. Verdauungs Krankheiten*, 1901, vol. vii., p. 501) reports two new instances of chronic diarrhœa apparently dependent upon the presence of balantidium coli. He has observed altogether eight similar instances. In five of these cases a rapid recovery followed the disappearance of the parasites. In one case with severe symptoms and a great number of balantidia in the stools there was an early improvement, but the patient failed to continue the treatment. In another instance recovery began about a month after the disappearance of the parasites, and in a third the diarrhœa continued despite the disappearance of balantidia. In this case, however, there had been a chronic colitis of two and a half years' duration before the beginning of the

treatment. The author believes that during this time the intestine had suffered changes sufficient to account for the duration of the symptoms. He concludes: "One is fully justified in assuming that in these cases balantidia were the cause of the diarrhœa, and that the main indication in the way of treatment is their destruction."

In all of these cases the treatment advised by Waldenstroem and Henschen, namely, large enemata (2500 c.c.), to which 50 to 75 c.c. vinegar and 5 to 7.5 tannin were added, resulted in a rapid disappearance of the parasites.

Recent observations appear to have settled beyond a doubt the question as to the pathogenicity of this parasite.

STRONG and MUSGRAVE (*Bulletin of Johns Hopkins Hospital*, 1901, vol. xii., p. 31) report from the Philippines a case of diarrhœa resulting fatally in four months, in which the stools contained great numbers of balantidium coli. The blood showed an increase in the number of eosinophilic cells. At necropsy the lower part of the jejunum and ileum were reddened and contained considerable mucus. In the large intestine the mucosa throughout was reddened and covered with bloody mucus; there were also a number of shallow ulcers. Balantidia were demonstrated throughout the mucosa and passing through the submucosa and muscularis.

A most elaborate study of this question is that of SOLOWJEW (*Centralblatt f. Bakt.*, 1901, vol. xxix., pp. 821, 849), who has also demonstrated that balantidium coli may enter into the healthy mucosa between the glands. "Making their way further into the submucosa they increase markedly and bring about there also extensive changes. Hence, they penetrate the muscularis mucosæ between the muscle bundles. The most marked changes being observed in the submucosa, the necrosis begins here. This spreads in all directions, reaching on the one side the muscular coat, on the other the mucosa. The glands deprived in this spot of their proper nourishment become necrotic if they have not already been destroyed by the parasites.

"Thus, the general opinion that balantidium coli is met with only on the surface of the mucosa, where it feeds upon the mucus, cannot be considered correct. The presence of the parasites in the depths of the tissues explains the malady produced by them, as well as the tendency to frequent relapses after their apparent complete disappearance."

This article is accompanied by a full table of references.

[There would appear to be little specific in the clinical manifestations of these cases which, in some instances, present the symptoms of a chronic diarrhœa, in others of an acute dysentery, with mucus and bloody dejecta. The reviewer has seen some of Strong's specimens which are convincing as to the pathogenicity of the parasite.—W. S. T.]

The Etiology of Acute Dysentery in the United States.—Under the direction of FLEXNER, VEDDER and DUVAL (*Journal of Experimental Medicine*, 1902, vol. vi., No. 2, p. 181) have undertaken to solve two problems: 1. To determine by comparative study whether the organisms described by Shiga in Japan, by Flexner and Strong in the Philippines, and by Kruse in Germany are of the same species, and 2, to discover the cause of acute dysentery in the United States, and if possible to identify it with the organisms of the observers mentioned. In other words, to determine

whether acute dysentery is the same the world over, and whether it be due to a specific organism, bacillus dysenteriæ Shiga.

After briefly describing their technique they state that before the organism under consideration can be considered to be bacillus dysenteriæ, it must have fulfilled the following requirements:

a. It must give the proper cultural characteristics, as shown by standard cultures of Shiga, Flexner, and Kruse.

b. It must possess the right morphology, as shown by the same.

c. It must give a positive agglutinative reaction with the same of the known dysenteric sera.

Their material was drawn from various sources. The bacillus dysenteriæ was grown from the stools of five different cases studied in various Philadelphia hospitals. It was also obtained in three cases of dysentery which occurred in the Lancaster County Almshouse and Insane Asylum, where several deaths from the disease had occurred. They also had the opportunity of studying a severe epidemic of dysentery which broke out in the Springside Home, New Haven, Conn. In this epidemic more than fifty cases occurred within three weeks among the 350 inmates, all being of a very acute form, with fatalities. They obtained the bacillus in fourteen of these cases which they studied. Three of these were insane patients.

They describe in detail the cultural characteristics, morphology, and agglutination reactions of the organism. The agglutination tests were made with the organisms obtained from Shiga, Flexner, Kruse, and Strong and with the organisms which they isolated from their own patients. The tests were made with the blood of the patients they observed, and also with a sample of antidysenteric serum sent by Shiga to Flexner. Briefly stated, the agglutination reaction was practically identical with all the organisms.

As a result of their study of the cases in this country, they firmly believe that there is a specific bacillus, and that it is identical with the organism described by the observers mentioned. They have no doubt that the organism is pathogenic. It is interesting to note, however, that in no instance have characteristic intestinal lesions followed inoculation of animals with the organism. Flexner and Strong have both produced typical dysentery in man following the ingestion of bacillus dysenteriæ.

It is important to note that the organism in this country has been found both in sporadic and epidemic cases; also that it is apparently the cause of acute dysentery in the insane. It is also present in the cases of "terminal" dysentery in association with chronic Bright's disease.

They draw the following conclusions from their study:

1. The several standard cultures used in this study are indistinguishable—a conclusion previously reached and stated by Flexner.

2. The acute dysentery of the United States is due to a bacillus indistinguishable from that obtained from the epidemics of dysentery in other parts of the world.

3. The sporadic and the institutional outbreaks of acute dysentery are caused by some micro-organism, and this organism is identical with that causing epidemic acute dysentery.

4. The cause of acute dysentery, whether sporadic, institutional, or epidemic, is bacillus dysenteriæ Shiga.

A Case of Uræmic Ulceration of the Stomach and Small Intestines.—MATHIEU and ROUX (*Archives Générales de Médecine*, January, 1902, p. 14) remark on the infrequency of ulceration of the gastro-intestinal tract in uræmia. They report a most interesting case which came under their personal observation and which terminated fatally. The patient was a young woman, aged twenty-two years, who was admitted to the Andral Hospital, Paris, suffering from symptoms which, on admission, were thought to be due to advanced pulmonary tuberculosis. Later it was learned that she had been in various hospitals during the previous three years, suffering from chronic nephritis, and the urine on this admission was found to be loaded with albumin. The patient's main complaint was severe abdominal pain. This was most marked in the right iliac fossa. On palpation of the abdomen it was found that there was marked muscular rigidity. There was no distention of the abdomen, nor was there any nausea, vomiting, or hiccoughing. The patient failed rapidly, and died a few hours after admission. The autopsy showed marked chronic interstitial nephritis, with hypertrophy of the heart. The most interesting findings were in connection with the gastro-intestinal tract. Along the lesser curvature of the stomach there were six ulcerations of the mucous membrane. One was large, measuring 3 by 4 cm., and presented all the features of an ordinary round ulcer, and was much deeper than the others. The remaining five were much smaller and more superficial.

There was quite an extensive ulceration of the smaller intestine, reaching from the point 4 to 5 cm. from the ileo-cæcal valve for a distance of 75 cm. The ulceration was situated along the free border of the intestine. Over this area there was no marked loss of substance, but its surface was covered with a yellowish diphtheric-like exudate. This long ulcerated area seemed to have been formed from a series of separate ulcers, measuring from 15 to 20 mm. by 2 to 6 cm. There were no ulcers found in the large intestine.

The authors in a search of the literature have collected 22 cases in which there have been ulcerations in some part of the gastro-intestinal tract in connection with advanced cases of Bright's disease. The majority of the cases have been in patients from eighteen to twenty-five years of age. In 20 of the 22 observations definite reference to the age is made. In 13 of these the ages range between fourteen and twenty-four years. In 10 of these 13 cases the ulceration was in the ileum, near the cæcum; in 1 the stomach was involved; and in 2 the large intestine showed more or less extensive ulceration.

The ages of the 7 other patients ranged between thirty-two and forty-seven years. Of these 3 had hemorrhagic erosions of the stomach, and in 4 the large intestine showed less numerous ulcerations. In none of these 7 cases was the small intestine involved. The ulceration of the small intestine appears then to be more frequent in young individuals.

In practically all the cases the ulceration was not suspected during life. All the abdominal symptoms which have been present in these cases have also occurred in nephritic cases without intestinal ulceration. In the majority of cases there has been severe diarrhœa, the stools being at times hemorrhagic. In a few instances constipation has occurred. Abdominal pain is not a constant symptom. It is worthy of note that in 2 cases, those

of Méry and Barbe, perforation had occurred, with resulting peritonitis. The writers consider the complication a most grave one from a prognostic stand-point, stating that nearly all the cases terminate fatally within from a few days to a few months. They believe, however, that recovery may occur after ulceration has once occurred, owing to the fact that in some of the cases reported many healed ulcers have been found. They were not able to establish definitely that the ulcerations were due to infarction of the bloodvessels supplying the areas involved. They seem inclined to the view that they were due to the result of toxic substances circulating in the blood. They state that the large gastric ulcer was practically indistinguishable, either by gross or microscopical examination, from the ordinary round ulcer of the stomach, and they consider it of interest to find that a typical round ulcer may occur in Bright's disease and be apparently due either directly or indirectly to this condition.

SURGERY.

UNDER THE CHARGE OF

J. WILLIAM WHITE, M.D.,

JOHN RHEA BARTON PROFESSOR OF SURGERY IN THE UNIVERSITY OF PENNSYLVANIA, SURGEON TO THE UNIVERSITY HOSPITAL,

AND

F. D. PATTERSON, M.D.,

SURGEON TO THE DISPENSARY OF ST. AGNES' HOSPITAL, ASSISTANT SURGEON TO THE DISPENSARY OF THE UNIVERSITY HOSPITAL.

A Case of Excision of the Vesiculæ Seminales for Primary Tuberculous Disease.—HODGSON (*British Medical Journal*, November 16, 1901) reports the case of a man, aged thirty-two years, married, who presented himself for treatment for frequent and painful micturition of three-years' duration. On an average he micturated at half-hour intervals day and night, but just previous to his admission to the hospital this interval was increased to five minutes. The pain, which was cutting in character, always shot from his perineum to the end of the penis, always preceded micturition and increased in intensity as the desire to micturate increased. No family history of tuberculosis could be obtained, and the previous venereal history was also negative. Examination showed the prostate to be normal in size; but there was an irregular, nodular mass, firm to the touch and hardly the size of the little finger, which could be detected on the right side of the base of the bladder. This swelling commenced immediately above the prostate, and extended upward, backward, and slightly outward, but the prostate itself was normal in size. The urine was negative except for tubercle bacilli. Operation being decided upon, the patient was chloroformed and placed in the lithotomy position. A sound was introduced into the bladder, the sphincter ani stretched, and then a semilunar incision three inches long was made across the perineum one inch in front of the anus. The dissection was continued until the seminal vesicles

were exposed, ligatures were suitably placed and both vesicles were removed in their capsule. The wound was closed except for a gauze drain. The patient made an uninterrupted recovery.

The Surgical Treatment of Sciatica.—HALLEY (*The Scottish Medical and Surgical Journal*, February, 1902) reports five cases of sciatica treated by stretching, which were relieved of pain almost immediately after the operation. Relief from pain is known to have continued for four months in two cases and thirteen months in one. In one of these it had existed for eight years before the operation. In one case, where no subsequent history has been obtained, relief followed the operation, although sciatica had existed for the previous five years. The sheath should be opened only if there is much effusion, otherwise simple stretching is sufficient. The author believes that from the relief after nerve-stretching, which results in even long-standing cases, this treatment ought to be adopted sooner. Many of these chronic cases treated with numerous drugs and external applications would benefit more from prolonged rest, but many cannot carry this out. Provided the cases are limited and well defined, having no other pains and no other organic condition in pelvis or elsewhere, nerve-stretching is beneficial, and should be recommended early. Should the pain recur, after operation, in the limb below the knee the author recommends further nerve-stretching lower down.

Intubation.—KUHN (*Centralblatt f. Chir.*, December 28, 1901) states that the instrument used by him for this purpose is most simple, being a metal cylindrical pipe or tube. In order to introduce this tube into the larynx and trachea a guiding tube is first introduced. This should be bent in a half circular form, like a metal catheter. In order to secure the tube outside of the mouth after its introduction, the author recommends the application of a diagonal piece of metal like the shield of a tracheotomy canula, which can be maintained in position at the corner of the mouth by a rubber band which encircles the head. To this band should be attached a thick piece of rubber which should be placed between the teeth, and so prevent the teeth from coming in contact with the tube under all circumstances. The indications for intubation are many—in the removal of tumors of the throat, or during any operation under anæsthesia there may arise a necessity demanding its use. The technique of intubation is so simple that every surgeon may attempt it without fear. In intubation of a grown person it is sufficient to draw up the epiglottis quickly, then to grasp or press the underside of the epiglottis with the left forefinger, and then allow the tube to slide along the under side into the larynx. Gentle pressure or a slight rocking motion of the tube from side to side will materially help in the introduction. As the tube is introduced the guiding tube should be gently removed. Unless the patient be fully anæsthetized some cough is caused by the irritation of the foreign body, or sometimes a sense of suffocation as the result of an excess of mucus lodging in the trachea. Cocaine or antipyrine will relieve the irritation, and the excessive mucus may be left to take care of itself. The largest tube that can be successfully introduced is the best. An important point that should not be neglected is to keep the tube thoroughly free from mucus by wiping it out with a small swab or brush. The chief indications for intubation are:

1. Compression of the trachea from any cause; and it is to be preferred to tracheotomy in operations on goitres, for the reason that the anæsthesia may go on in its natural way, the tube may be removed immediately after the operation; and, most important, there is no danger of infection of the wound as there is when tracheotomy is performed. 2. There is no danger of blood flowing into the air-passages, as may happen in tracheotomy. 3. In case of asphyxia the air may be forced through the tube by a bellows, and, as a rule, this will quickly be followed by relief.

Practical Observations on Appendicitis.—LLOYD, (*Birmingham Medical Review*, December, 1901) states that he should like to see a closer and more constant association of the words "peritonitis" and "cellulitis" with that of "appendicitis," so that the public might in time learn that it is the peritonitis or the cellulitis which constitutes the serious elements in this disease, and not appendicitis itself, and that the one is likely to follow on the other at any time and with every degree of severity; and they would then better interpret the attitude of the profession toward the disorder, certainly as regards the employment of medicines on the one hand and of operations on the other. Inflammation within the appendix is not necessarily attended by symptoms of any kind so long as the products of the inflammatory process are able to get out of it, pain being induced only when more or less obstruction exists to the easy escape of these products into the lumen of the bowel, and in this factor of obstruction chiefly lies the key to the whole subject of appendicitis. What the appendiceal obstructions are, how they originate, and how they give rise to trouble, may be classified under the heads of strictures, kinks, occlusions, and foreign bodies—under which term is included fecal concretions. Strictures may occur in any part of the appendix, of every degree of tightness, and may be either congenital or acquired. The congenital are by far the more common. Acquired strictures may be either simple or specific—the former the result of chronic inflammation, and the latter of ulceration of the mucous lining and subsequent cicatrization.

The etiology of the simple form of acquired stricture here is precisely that of the better known but less common stricture of the urethra, except that it is not due to gonorrhœal inflammation. It results from a chronic inflammatory process affecting the mucous membrane, extending gradually into the submucosa, and generating there a fibrosis of the connective tissues; it is contractile and constant. This form of inflammation within the appendix occurs usually by extension from the lining of the great intestine. The strictures due to specific causes follow on ulceration, and the types of ulcer met with in the appendix are similar to those which affect the intestine in its neighborhood, viz: typhoid, dysenteric, tubercular, syphilitic, and carcinomatous.

Kinks or twists of the appendix are usually congenital and obstruct by the "chokage" which results in every soft-walled tube when it is actually bent or twisted upon itself in any direction.

Occlusions of the appendix are where the canal of the appendix is organically obliterated in a part only of its length, so as to leave on the distal side of the obliteration a closed cavity lined by mucous membrane, more or less normal. Inflammatory effusions within such cavities are practically abscesses

ab initio, as they cannot empty themselves along the appendix into the cæcum; their contents can only escape by bursting into the peritoneal cavity the intestines, or the adjacent cellular tissue.

Foreign bodies, the majority of which are fecal concretions, may both irritate and obstruct. They become obstructing agents when they endeavor to escape along the proximal part of the canal toward the cæcum. They may block up the outlet of the organ just as the gallstone does the cystic duct, or a renal calculus the ureter, and the cavity of the appendix on their distal side then becomes distended by its own products. The consequences of this increasing distention constitute the real dangers of "appendicitis," and vary in their kind according to the distensibility and position of the appendix and the character of the inflammation by which it is affected. The signs and symptoms of appendicitis are many and varied, but the author lays particular stress upon pain and inflammatory swelling. The pains of appendicitis are due to two distinct conditions—distention of the appendix and inflammation of the peritoneum or cellular tissue. The first always precedes the others, and differs from them in character and in locality. They are, however, quickly merged together in the ordinary type of case, and it requires, therefore, careful and early investigation to discriminate between them. Appendicular pain is not always severe at its first onset, and is not often referred to the appendix region. It is frequently felt on waking in the morning, and is commonly epigastric in position. Usually within twelve hours, however, it extends to the iliac region Continuous severe aching pain during the early days of the attack is of grave moment, and is typically seen in the acute gangrenous form of the disorder. It is due to obstruction of the appendix, is temporarily diminished when the organ gives way, and is shortly followed by the more paroxysmal pains of peritonitis

Heat, tenderness, hardness, and swelling are essential features of every inflammation, and must be present, therefore, in all cases of appendicitis. They may not always be appreciable by physical examination, but they are often overlooked when they are quite discoverable; and inasmuch as the "presence of a tumor" is the chief diagnostic sign of the affection we are discussing, it is necessary that we should give great attention to this feature in our examination. Although the base of the appendix is fairly constant in its anatomical position, the tip of the organ may swing in any direction, and the tumor, therefore, which attends or results from its inflammation may develop at any part within reach of the appendix; for working purposes we may describe them as iliac, pelvic, lumbar, abdominal, and retrocæcal.

Fortunately for our patients, iliac swellings are the most common and are easily palpable in the right iliac fossa, and their diagnosis is simple enough; but when the iliac tumor is absent diagnosis is a less easy matter; careful examination, however, will nearly always reveal the presence of swelling in one or other of the positions already named.

The pelvic variety lies in Douglas' pouch and can be felt by examination from below, either per rectum or vaginam, when absolutely nothing is to be discovered by palpation through the abdominal wall. Rectal or vaginal examination should be a routine procedure in every case of inflammatory abdominal disease.

The lumbar variety lies deep in the lumbar region, sometimes extraperi-

toneally in the connective tissue behind the bowel and below the kidney, and sometimes intraperitoneally outside the ascending colon. It is easily overlooked, particularly in well-developed or stout people; a distinct tumor cannot always be made out, but a comparative examination with the region of the opposite side readily reveals the presence of "fulness."

The abdominal variety may be situated in the epigastric, hypogastric, or right hypochondriac regions, often in the neighborhood of the umbilicus, either above, below, or to either side of that structure. Careful comparative palpation cannot fail to disclose such swellings.

The retrocæcal variety is next in frequency to the iliac, and lies at the back of the cæcum, at the level of the pelvic brim and opposite to the sacro-iliac joint. It can be felt only on deep backward palpation rather as a fulness than a distinctly localized tumor. It is usually resonant on percussion for the reason that the head of the cæcum lies in front of it, and is often mistaken for feces in the large bowel. A finger passed high up in the rectum and to the right sometimes appreciates the lower limit of the inflammatory area.

There is one type of appendicitis in which "tumor" is conspicuously absent, viz.: the acute gangrenous or perforative variety, with widespread peritonitis, where everything is lost in the general abdominal distention; although in these cases a tumor formed by the distended appendix can usually be felt before rupture has taken place.

On the question of treatment there is still something to be learned. At the commencement of an attack it is necessary to clear out the bowel; calomel and castor oil are the best remedies, followed by salines and belladonna. The question of operation should be considered from the very outset of the attack, because if it is to be of service in some of the varieties of the affection it must be performed within the first thirty-six hours. In those cases in which the indications for operation are in doubt operation is the safest alternative. Operation having been decided upon, the incision should be made over the tumor except in the pelvic variety, where no tumor is palpable, but there is fluctuation in Douglas' pouch, when the incision should be made through the posterior vaginal fornix in women, and through the rectum in children and men.

For the drainage of appendiceal suppurations there is nothing better than the rubber tube surrounded by a packing of iodoform gauze. The tube may be withdrawn early, and the gauze comes away usually within a week, and may be renewed if necessary. A narrow single strip carried lightly into the depths of the wound is all that is required—there is no need for the painful stuffing so often seen.

Great care should be given to the suture of the parietal wound, even where drainage is arranged for. This can be best done by interrupted fishgut sutures passed carefully through all the layers of the abdominal wall. This thoroughness can only be secured by seeing that each separate layer in the sides of the wound is systematically transfixed by the needle.

The appendix should always be removed if it comes readily to hand, but it is safer to leave it if there is likely to be much separation of adhesions in getting it away. When it is left behind, a few days after operation it occasionally happens that feces appear in the discharge from the wound, and anxiety as to the soundness of the cæcal wall is often felt, but usually the

feces come through the open stump of the appendix, and no harm follows, the majority healing soundly in the end.

Operation especially done for the removal of a diseased appendix during an interval between attacks has become a well-established procedure, and its results are extremely satisfactory; as a rule, it is best done through the oblique iliac incision. The after-treatment of appendiceal operations is that common to the general run of abdominal sections.

A Table for Operations upon the Stomach and Liver.—KELLING (*Centralblatt f. Chir.*, October 19, 1901) states that every surgeon has often experienced difficulty in operations upon the upper portion of the stomach and liver for the reason that this region is so hidden by the arch of the ribs as to be almost inaccessible. Lannelonge has proposed his rib-resection method for cases of this character, but this method is inadvisable, as it means an added risk to the patient, and does not always produce the desired result. For this reason it is of material assistance to devise a posture which would render the diaphragmatic region accessible to the eye as well as to the hand. The posture devised by the author imitates that which anatomists use when they wish to prepare the muscles of the diaphragm. They lay the body with the trunk horizontal, but bent to nearly a right angle in the lumbar region, so that the pelvis and legs hang downward and the feet touch the floor. The portion of the table on which the trunk rests is movable. On the upper surface of this portion two buckles are placed through which a strap is fastened to hold the body in place. In order to obtain better access to the subphrenic region the usual median incision in the linea alba should be supplemented by an oblique incision starting at the apex of the twelfth rib and extending diagonally toward the median line. In order to keep the intestines in the abdomen a towel is placed over them below the stomach and its margins fixed with clamp-forceps. The central portion should be pressed down on the viscera by an assistant's hand, while with the other hand he pulls the ribs upward. When working in the subphrenic space the operation may often be facilitated by dividing the suspensory ligament of the liver.

Quinine as a Styptic and Antiseptic.—MARX (*Centralblatt f. Chir.*, 1901, No. 45) states that as the result of his experiments he recommends quinine as a styptic and antiseptic. Everybody knows quinine as a specific protoplasm poison. The author states that space does not permit him to describe the experiments which proved the antiseptic powers of this drug. The styptic powers of quinine arise from the ability of its salts to agglutinate the red blood-corpuscles. For practical use, the best preparation is a 1 or 2 per cent. solution of quinine hydrochloricum, which should be applied to the bleeding surface with a gauze compress or tampon. It is needless to state that its use should be confined to cases of parenchymatous bleeding. Careful observation has failed to show any injury to the tissues; in fact, no reaction of any kind was observed. The disinfecting power of quinine on infected wounds is but slight, but in aseptic wounds it absolutely stops parenchymatous bleeding and has the additional power of rendering innocuous any germs that may have been conveyed into the wound by the operator's hands.

THERAPEUTICS.

UNDER THE CHARGE OF

REYNOLD WEBB WILCOX, M.D., LL.D.,

PROFESSOR OF MEDICINE AND THERAPEUTICS AT THE NEW YORK POST-GRADUATE MEDICAL SCHOOL AND HOSPITAL; VISITING PHYSICIAN TO ST. MARK'S HOSPITAL,

AND

SMITH ELY JELLIFFE, M.D., PH.D.,

PROFESSOR OF PHARMACOGNOSY AT THE COLLEGE OF PHARMACY; CLINICAL ASSISTANT AT THE VANDERBILT CLINIC (COLUMBIA UNIVERSITY), NEW YORK.

Contribution to the Knowledge of Phloridzin Diabetes.—DR. O. LOEWI has been experimenting to establish the fact, already determined by von Mering, that subcutaneous injections of phloridzin are followed by a greater excretion of sugar than when the drug is taken by the mouth. In the repeated experiments he found, as the cause of this peculiarity, (1) that the absorption of the phloridzin in the intestine is not a complete one, but that a decomposition takes place there, whereby a product is formed, difficult of absorption, yet capable of inducing diabetes if brought directly into the blood. The proof of this lies in the fact that if an extract of the feces of a dog fed with phloridzin be injected into another animal, glycosuria will follow; (2) in order to insure the highest degree of glycosuria, a certain amount of phloridzin is required, and, no matter how much this is increased under like conditions, no more sugar will be voided. If, however, the amount of food capable of producing sugar be increased, the amount of phloridzin must be larger to insure a maximum excretion; and (3) changes in the temperature of the animal are of no appreciable effect upon the glycosuria.—*Arch. für exp. Path. u. Pharmak.*, 1902, Band xlvii., p. 48.

Action of Digitalis and Its Allies upon the Vessels.—DRS. R. GOTTLIEB and R. MAGNUS have been repeating the experiments of F. Pick, which had been considered to prove conclusively a direct constricting action of digitalis and similar drugs upon the bloodvessels. This investigator did not give any evidence of the part played by the different vessels in this process, nor upon the time the vasomotor effect takes place and its duration. The new experiments were conducted on dogs. Two entirely different methods were employed: in one the amount of blood flowing out of the veins of different regions was registered after a sufficient amount of atropine had been given to overcome the slowing of the pulse; in the other the plethysmograph was used. The experiments showed that the increased blood pressure was due to increased heart action and contraction of the vessels, and that the latter is due to peripheral action which, in case of digitoxin, is general. In the case of the other examined glycosides (digitalin, convallamarin, strophanthin), the action is restricted to the splanchnic area. There is, however, some active constriction going on here in the peripheral vessels, yet this is overcome by a passive dilatation owing to reflux of blood from the intestines and an active reflex dilatation set up by the splanchnic

contraction. The general narrowing of the pathway of the blood seen with digitoxin gives a high resistance, which must be overcome by the heart; strophanthin, etc., open the vessels of the periphery, and this materially relieves this organ.—*Archiv für exp. Pathologie u. Pharmakologie*, 1902, Band xlvii., p. 135.

The Influence of Carbon Dioxide Inhalation upon the Body Temperature.—Dr. N. von Westenryk, to determine what effect the inhalation of small amounts of carbon dioxide would have upon the body temperature, employed rabbits with normal temperature and such in which an artificial fever had been induced by punctures of the heat centres. The animals were placed in an air-tight chamber in which some of the air was substituted for oxygen, and the experiments were conducted with 3 per cent. of volume of carbon dioxide gas. General symptoms did not appear except a slight acceleration and deepening of the respiratory movements at first, and a remarkable quietness of the animals. Within the first thirty to forty minutes the temperature dropped 0.4° C. to 1° C. and then again slowly reached the normal, even if they were brought back into the box. In the animals with fever the same observations were made, except that the reduction was 1° C. to 2° C.—*Archiv für exp. Pathologie u. Pharmakologie*, 1902, Band xlvii., p. 82.

Active Principle of Guaiacum.—Dr. E. Schaer has found that the antisyphilitic, diaphoretic, antiarthritic, and emetic properties of guaiac depend solely upon the saponin, which is most abundant in the bark, less so in the outer part of the wood, still less in the medulla, and least of all, yet in appreciable amounts, in the resin. The fact that the decoction of the wood contains the most saponin of all galenical preparations, and has been found to be the most active preparation for centuries, seems to support this theory, as do also the recent observations that other ingredients, such as guaiaconic acid, have no effect in syphilis. The author recommends that the saponin of the bark and wood be isolated in pure form, that they be compared with each other and other known forms of saponin, and that they be tried pure in the various affections for which guaiac is known to be valuable.—*Archiv für exp. Pathologie u. Pharmakologie*, 1902, Band xlvii., p. 127.

Arsenic and Beriberi.—Dr. Ronald Ross reports on the analysis of twenty samples of hair taken from Chinese patients afflicted by beriberi. Since it has been suggested that this type of neuritis might have something in common with arsenical neuritis, the results were suggestive at least. These analyses gave indefinite results as far as a causal nexus being established. In six positive evidence was given; yet this is of importance, especially since the recent cases alone were those that gave positive results; the results from patients with long-standing disease were negative. The exact site from which the hair was obtained was not recorded. As this is a matter of importance, the suggestion is offered for future study that samples should be taken from near the scalp.—*British Medical Journal*, 1902, No. 2145, p. 329.

The Effects and After-effects of Ethyl and Ethylene Bromide.—Dr. D. Scherbatscheff, after conducting a number of experiments, finds that there seems to be considerable difference between the physiological action of the ethyl bromide and the corresponding ethylene salt; for while the former seems to be relatively safe as an anæsthetic, the latter manifests many dangerous properties if used by inhalation. Indeed, many of the accidents reported are to be ascribed to the use of the wrong drug, owing to the great similarity of the names. To decide this point definitely, however, a number of experiments with frogs, white mice, and dogs were made. The frogs and mice were placed under a bell-jar, the dogs in an air-tight glass case, and a definite amount of ethylene bromide was allowed to evaporate. A real narcosis was induced only in frogs; and in all animals evil after-effects resulting in death were noted. The respirations were much increased and rendered shallow; there was a continuous sinking of the blood-pressure, and the cornea became opaque. Periods of excitation, convulsions, and vomiting also developed. The cause of death must be looked for in specific changes in respiration and circulation; the possibility that hydrogen bromide was formed and the blood thus acidified must be excluded, since in all cases it reacted alkaline. Dissection showed irritation of the bronchi, hyperæmia, and sometimes hepatization of the lungs and of the liver. Similar experiments conducted with ethyl bromide gave a pure narcosis which ended in death if continued long enough, but never did any ill-effects accompany the anæsthesia.—*Archiv für exp. Pathologie u. Pharmakologie*, 1902, Band xlvii., p. 1.

Upon the Toxicity of Dimethyl Sulphate.—Dr. S. Weber has thoroughly investigated the toxicology of dimethyl sulphate on animals. The use of dimethyl sulphate, a colorless, oily fluid of a specific gravity of 1.33 and a boiling-point of 370.4° F., has recently become an extended one in chemical factories. These studies were taken up because of the fact that three cases of poisoning have been reported. Two of these ended fatally under marked local and pulmonary symptoms. A twofold action was found: one local, strongly caustic, and one general, upon absorption of the poison. The caustic effects are seen most intensely upon the respiratory organs and conjunctivæ, especially if the substance is heated so that free vaporization takes place; while if applied to the skin, or if given subcutaneously, hyperæmia and necrosis, and if given *per os*, general gastro-intestinal disturbance and perforation result. The general symptoms consisted of nystagmus and convulsions, increasing in frequency and intensity, then again diminishing, and ending in coma and paralysis, with accelerated respiration and unaltered heart action. The lethal dose was 5 centigrammes per kilo body weight in rabbits if injected, and death generally set in after several hours. The action of dimethyl sulphate does not depend upon its decomposition products, sulphuric acid and methyl alcohol, but upon a specific action inherent to the body itself. The caustic properties especially are peculiar to this compound, and are not found in the other ethers and esters of the fatty series, which are also incapable of setting up convulsions.—*Archiv für exp. Pathologie u. Pharmakologie*, 1902, Band xlvii. p. 113.

GYNECOLOGY.

UNDER THE CHARGE OF

HENRY C. COE, M.D.,

OF NEW YORK.

ASSISTED BY

WILLIAM E. STUDDIFORD, M.D.

Pigmentation of the Abdomen.—LEHMAN (*Revue prat. d'Obstétrique et de Pœdiatrie*, September, 1901) calls attention to the common error that the pigmentation in the median line of the abdomen is supposed to be found only in pregnant women. He shows that it may be observed in both sexes and at any age. Even in young children it may appear in connection with inflammation of the intestines, typhoid fever, and tuberculosis, while it is often marked in healthy girls at the time of puberty. The discoloration in the latter is probably due to the general congestion of the pelvic organs, and may be regarded as the forerunner of the first menstrual flow. If menstruation is regular and normal, the dark line disappears; if irregular and painful, it is apt to persist.

Among 122 young girls examined by the writer the line was present in 66. Of these 26 suffered from amenorrhœa, 20 from dysmenorrhœa, and 14 from menorrhagia; 6 had obstinate constipation and abdominal pains. The other 56 patients menstruated regularly without pain, and had no intestinal disturbances.

After the climacteric the line of pigmentation is barely visible.

Genital Atresia.—LABUSQUIÈRE (*Annales de Gynécologie et d'Obstétrique*, No. 8, 1901) believes that the majority of atresiæ are acquired, and hence that it may be possible to prevent them. He advises that not only should a routine examination of the external genitals of the newborn be made, especially where the mother has a gonorrhœal discharge, but that prophylactic treatment should be adopted in the shape of antiseptic lotions. The same solution of nitrate of silver which is instilled into the eyes may be used with advantage.

So-called precocious menstruation is always to be regarded with suspicion as a possible evidence of gonorrhœal infection, and an examination should be made to ascertain if the latter is present. Cases of persistent leucorrhœa in little girls may result in atresia, so that it is advisable to prove its absence by the careful introduction of a sound.

Prolonged absence of the catamenial flow in girls at the age of puberty may justify an examination, especially if there is a history of a previous infection. The presence of menstrual molimina, or even vicarious hemorrhage, does not contraindicate such an investigation.

Referring to the development of hæmatosalpinx in connection with genital atresiæ, the writer affirms that when the enlargement of the tube is due to

simple retention of blood and is not of inflammatory origin, as shown by the absence of any history of acute infection, of constitutional disturbance, or of persistent abdominal pains, primary laparotomy is not justifiable. It is better to first evacuate the retained blood per vaginam if possible, abdominal section being performed later if necessary.

Infection of Abdominal Wound during Operation.—PEISER (*Monatschrift für Geb. u. Gyn.*, Band xvi., Heft 2) states that even in cases of benign adenocystoma of the ovary cells from the fluid may be transplanted to the abdominal wound or to the site of a trocar puncture, from which growths develop similar in character to the parent tumor. These may grow internally into the intestine and externally through the skin, and these secondary growths may become cancerous. The writer infers from this fact not only that explorative puncture or tapping of ovarian cysts is a dangerous procedure, but that during operation the edges of the wound should be carefully protected before the contents of the cyst are evacuated, especially if thick and gelatinous.

SCHAEFFER (*Zeitschrift für Geb. u. Gyn.*, Band xlv., Heft 3) reports a case of ovariotomy in which the tumor was found to be an adenocarcinoma. A recurrence occurred which was confined entirely to the cicatrix, the pelvic and abdominal cavities being healthy. He infers that the wound was inoculated at the time of operation.

Fixation of the Prolapsed Uterus.—BUCURA (*Zeitschrift für Geb. u. Gyn.*, Band xlv., Heft 3) reports sixteen cases from Wertheim's clinic with only one failure. Briefly, the operation practised by the latter consists in denuding an oval surface on the anterior vaginal wall, extending as low as the meatus urinarius. The fundus uteri is drawn down through an opening in the anterior vaginal fornix and is sutured to the surface in question; then the pelvic floor is repaired.

The advantages claimed are prevention of a recurrence of the cystocele, which is the cause of failure in most operations for prolapsus. Menstruation persists and there is a free discharge of the uterine secretions. Marital relations are not interfered with. However, it is important that conception should not occur, which in younger women can be secured by resecting the tubes. In general this plastic operation is preferable to hysterectomy in intractable cases.

Conservative Treatment of Fibromyomata.—OLSHAUSEN (*Zeitschrift für Geb. und Gynäkologie*, Bl. lxiii., Heft 1) pleads for the more general adoption of myomectomy instead of supravaginal amputation of the fibroid uterus, especially in women under forty. He does not hesitate to leave small nodules, which may never give any future trouble. While the operation of enucleation in former years was a dangerous one, now it is quite safe, especially if the bed of the tumor is carefully sutured with catgut.

In 207 myoma operations he had 29 enucleations without a death. As regards the number of cases of fibroid in which interference is called for, the writer notes that in 200 cases in private practice he found it necessary to operate in only 33. During the three years from 1897 to 1900 320 private cases were seen, in only 53 of which was an operation indicated. He believes

that probably 18 per cent. really require operation, which is not yet entirely free from unavoidable dangers, especially embolus and intestinal obstruction.

Ultimate Results of Operations for Uterine Fibroids.—BURCKHARD (*Zeitschrift für Geb. und Gynäkologie*, Bd. xliii., Heft 1) finds, from an analysis of the statistics of a number of operators, that with few exceptions the results of myoma operations are quite satisfactory. After castration hemorrhage usually ceases if all the ovarian tissue has been removed; the tumor ceases to grow and usually diminishes in size. Menstrual molimina rarely persist after the removal of both ovaries, but may do so if one ovary is left, even if the uterus is removed. When the entire uterus is removed, with or without the adnexa, disturbances are less frequent than after castration and supravaginal amputation; if the ovaries are left they are still more rare. The writer has never observed profound psychical disturbances after the removal of both ovaries.

Since no injury to the health results from the presence of the ovaries after hysterectomy, and climacteric phenomena are less marked, they should always be preserved when they are healthy.

The Early Diagnosis of Uterine Cancer.—ABEL (*Archiv für Gynäkologie*, Bd. lxiv., Heft 2) calls attention to a peculiar arrangement of the elastic fibres in and around malignant foci which, he believes, constitutes an important diagnostic point in doubtful cases. Under a low power of the microscope these fibres appear to surround the cancerous alveoli, but under higher powers they are seen crossing in all directions between the cells, where they present a peculiar broken appearance, as if they were actually destroyed by the disease, instead of being merely pushed aside. These broken fibres are never seen in any other neoplasm of the uterus, such as condyloma or tuberculosis, nor in hyperplasia of the connective tissue, hence they serve to distinguish simple atypical epithelial growths from true carcinoma.

Ligation of the Ureters.—FRAENKEL (*Archiv für Gynäkologie*, Bd. lxiv., Heft 2), from experiments on rabbits, arrives at the conclusion that ligation of the upper end of a ureter after section of the duct does not always prevent the escape of urine from the kidney, as the ligature is apt to slip. Since in exceptional cases it may not be possible or justifiable to perform anastomosis of the ureter, it is important to be able to ligate it in such a way as to prevent slipping of the ligature. The writer advises that after ligation the upper end be sutured in the abdominal wound. If the urine escapes, the fistula can be cured by a subsequent operation; if the ligature holds and hydronephrosis of the corresponding kidney occurs, the patient still has a good chance of recovery, as shown by several reported cases. If the opposite kidney is diseased or uræmic symptoms appear the ligature can at once be divided.

Hæmatocele Due to Hemorrhage from the Ovary.—GABRIEL (*Archiv für Gynäkologie*, Bd. lxiv., Heft 2), in reporting a case of hæmatocele due to follicular hemorrhage in which the diagnosis of ruptured extra-uterine pregnancy had been made, reviews the literature of the subject. He finds

no satisfactory statistics with regard to the etiology of hæmatocele, ectopic gestation being regarded as furnishing about 28 per cent. of the cases. Authentic cases of ovarian hemorrhage in which the diagnosis was confirmed by operation are comparatively few in number, but none the less the condition is well recognized.

Hysterectomy for Cancer of the Uterus.—JORDAN (*Zeitschrift für Geb. und Gynäkologie*, Bd. xlv., Heft 21), after reviewing carefully the statistics of abdominal hysterectomy, arrives at the following conclusions: Vaginal hysterectomy is the natural method of removing cancer of the uterus when the disease is confined to that organ. Since the mortality by the abdominal route is three to four times that by the vaginal, and the operation is much more difficult, the indications for vaginal hysterectomy should be extended. The abdominal operation should be performed only when it is impossible to remove the uterus per vaginam, as in cases in which carcinoma is complicated by fibroid or ovarian tumors. If the pelvic connective tissue is so infiltrated that radical vaginal extirpation cannot be performed, there is no object in resorting to abdominal.

Vesical and Ureteral Fistulæ following Vaginal Hysterectomy.—HENKEL (*Zeitschrift für Geb. und Gynäkologie*, Bd. xlv., Heft 2) finds that the majority of injuries to the urinary tract occur during operations for cancer of the cervix uteri, rather than of the portio. As shown by Mackenrodt's statistics, the bladder and ureter are especially liable to injury during igni-extirpation, but the clamps have been responsible for many cases.

In 263 hysterectomies at the Berlin clinic previous to 1897 the mortality was 5.13 per cent., while the bladder was injured seven times, and one ureter was injured or tied in five cases. After the latter year, when the indications for the operation were extended to include cases in which the broad ligaments were infiltrated, in 375 cases (with a mortality of 5.06 per cent.) the bladder was injured fourteen times and the ureter nine times.

The writer finds that these accidents (especially to the ureter) have increased in number, especially when clamps are used. The prognosis in wounds of the bladder is good, about 68 per cent. healing when sutured at the time.

Hot Air in the Treatment of Pelvic Exudates.—KEHRER (*Centralblatt für Gynäkologie*, 1901, No. 52), in view of the fact that at least 95 per cent. of all pelvic exudates tend to become absorbed, emphasizes the importance of assisting natural processes by the use of such agents as reduce local hyperæmia. He uses hot vaginal douches several times daily, allowing at least three gallons of water to flow through a double-current glass tube, as well as hot sitz-baths and compresses applied to the lower abdomen. He speaks highly of the apparatus devised by Polano, in which continuous heating is effected by electricity.

THOMSON (*Ibid.*) commends the method of treatment introduced by Polano, with which he has obtained striking results in cases of chronic perimetritis. Not only is pain promptly relieved, but exudates are rapidly absorbed. The only contra-indications are advanced cardiac lesions or disease of the arteries.

OBSTETRICS.

UNDER THE CHARGE OF

EDWARD P. DAVIS, A.M., M.D.,

PROFESSOR OF OBSTETRICS IN THE JEFFERSON MEDICAL COLLEGE; PROFESSOR OF OBSTETRICS AND DISEASES OF INFANCY IN THE PHILADELPHIA POLYCLINIC; CLINICAL PROFESSOR OF DISEASES OF CHILDREN IN THE WOMAN'S MEDICAL COLLEGE; VISITING OBSTETRICIAN TO THE PHILADELPHIA HOSPITAL, ETC.

Hydroa During Pregnancy Caused by Staphylococcus Albus.—In the *British Medical Journal*, January 11, 1902, HOLMES and BULLOCK report the case of a patient in her third confinement who, on the day following the birth of the child, complained of severe itching in the palms of the hands and the soles of the feet. The tissues were red, and a thick confluent rash, the size of peas, was present. A similar eruption was seen upon the thighs, chest, and back. The patient had no fever.

On inquiry it was learned that in her other confinements the patient had suffered in a similar way. An examination of the fluid from one of the recent spots of eruption was made, and a pure culture of the staphylococcus albus was obtained.

The patient improved daily, and the child, which continued to nurse, was entirely free from the eruption. The treatment consisted in giving saline mixture, with small doses of arsenic, internally. Later tablets of sulphur were used.

Pregnancy and Parturition in a Case Complicated by Advanced Tabes Dorsalis.—At the meeting of the Gynecological Society of Munich, MIRABEAU (*Centralblatt für Gynäkologie*, 1902, No. 5) reported the case of a patient in advanced tabes dorsalis, who passed through pregnancy and labor.

In books upon diseases of the nervous system various statements are made concerning the influence of this disease upon the pelvic organs. The statement is made by Leyden and Goldscheider in Nothnagel's *Handbook of Internal Medicine*, that menstruation proceeds regularly in these cases and that pregnancy and labor may also go on normally. As the disease advances the statement is made that the functions of the pelvic organs are also disturbed. Books upon obstetrics contain little information upon the subject. Litschkus (*Wratch*, 1885) reports the case of a patient, aged twenty-six years, who was confined nine years previously, and who for seven years had manifested symptoms of tabes dorsalis. Labor lasted five days, but terminated spontaneously and the patient made a good recovery. Mirabeau's case was aged thirty-four years, who had been under observation for three years. The patient's history showed that after the seventeenth year her menstruation became regular, and that soon after she was treated in a hospital for syphilis. After thorough treatment by inunction she made a good recovery. Five years afterward she married, but had no children. Nine years after her infection and four years after her marriage she was found to have tabes

dorsalis. Mirabeau was called to the case because the patient had severe hemorrhage from the genital tract. On examination the patient seemed well nourished. She had ceased to menstruate for two periods and had been bleeding for five days. An abortion seemed threatened. This, however, ceased under rest in bed, warm douches and an ice-bag over the abdomen. The patient was found to have well-established tabes dorsalis. Both lower extremities were paralyzed, the patellar reflex destroyed, ataxia was well pronounced, and sensibility much diminished. The pupils were narrow, with absence of reflex. There was great difficulty with the functions of the bladder and rectum. The patient was immediately put upon a vigorous anti-syphilitic treatment and made considerable improvement as a result. As pregnancy drew to its close the probability of spontaneous labor did not seem great.

Contrary to expectation, labor proceeded without the slightest evidence of pain. The amniotic liquid escaped at the beginning of labor. The cervix was considerably dilated at this time. The expulsion of the child occurred sixty-five minutes after the rupture of the membranes, and but seven pains actually occurred, five of great length and two of short duration. The patient had not the slightest feeling from the uterine contractions. At the last the abdominal muscles contracted once, and the patient said that she felt as if the rectum was emptying itself easily of its contents. She had been without sensation in the rectum for several years. With the sixth pain the child, a well-developed girl, was born, and with the seventh pain the after-birth. The mother was not aware that she had given birth to a child until she heard its cry and saw the infant. The child did well and had a syphilitic eruption three weeks after birth, which subsided under the use of calomel. The patient made a good recovery from labor.

This extraordinary case illustrates remarkably the physiology of labor. It is a striking demonstration of the fact that the contractions of the uterus do not depend upon the ganglia of the spinal cord so much as upon the smaller ganglia upon the nerve trunks in the uterine structure. Evidently the transmission of sensation through the cord to the brain is a frequent source of delay in complicated labor. It is a familiar experience in dealing with patients that labor ceases through the reflex inhibition of suffering. When this is removed by disease or by an anæsthetic labor goes on regularly and independently.

Harelip.—In the *Archives of Pediatrics*, February, 1902, RACHFORD reports the following interesting and extraordinary case:

The parents in question have a family history of tuberculosis. Their first child, a girl, was born with a cleft of the upper lip and nostril and hard and soft palate. The second child, also a girl, had a similar deformity. The third child, a boy, was without deformity, but died subsequently of tuberculosis. The fourth child, a girl, was so terribly deformed that the child lived but a few hours. The fifth child was a boy, perfect in development, dying of tubercular meningitis shortly after he was two years old. The sixth pregnancy resulted in the birth of a girl with double harelip, afterward remedied by operation, the child dying of tuberculosis at eighteen months. The mother then became tuberculous, but improved on removing to another climate. Her

seventh child was a boy, perfect in development, and at the time of writing was thriving well.

A review of the case shows the fact that there is no family history of harelip or cleft palate. The mother has a highly arched palate. There is a very bad family history of tuberculosis. The four girls had cleft palate and harelip, and the three boys were entirely free from this deformity. The first and second boys died of tuberculosis, and the third is too young to have had much opportunity to acquire the disease.

Repeated Rupture of the Uterus.—In the *Monatschrift für Geburtshülfe und Gynäkologie*, 1902, Band xv., Heft 1, KRIWSKI reports the case of a patient, aged thirty-three, who had been pregnant five times, having borne three living children, one abortion, and on one occasion a deformed child. The pelvis was justo-minor with considerable flattening. The patient considered herself at full term. The membranes ruptured at the beginning of pains. Upon examination the heart sounds were not heard, the uterus admitted three fingers, and the child was presenting in the usual manner. The head had entered the pelvis, the pulse of the mother was somewhat rapid, and she seemed impatient and suffering considerably. There seemed to be no essential reason for terminating the parturition at that time. Some twelve hours afterward the abdomen was considerably enlarged and very sensitive. The patient was apathetic and had a sighing respiration. Contractions of the uterus were weak, but could be plainly discerned. The mouth of the womb was smaller than formerly, and the head considerably higher and above the promontory of the sacrum. The internal conjugate was between 10 and 11 cm. The patient was anæsthetized and version performed. It was necessary to bring down both feet and to perforate the head to deliver the patient. Upon examining the uterus after delivery, it was found that a laceration of the tissues into the parametrium was present on the right side. The uterus contracted well, and there was no hemorrhage. The pulse was good; the patient roused speedily from the anæsthetic, and complained of pain in the abdomen, which was distending. The placenta came away soon after the birth of the child. The vagina was tamponed with sterile gauze, and the uterus was compressed by a pad and bandage. The gauze was removed after some time, when a rupture was found in the upper portion of the uterus which was well closed by uterine contractions. An exudate developed at the site of the tear, which gradually passed away. Twenty-four days after confinement the patient was discharged in good condition. She afterward reported for examination, when a hard, painful tumor was found three fingers above the pubic bone, while the uterus was hard, large, and somewhat sensitive. On the left side the uterine appendages were enlarged, and there was a remnant of parametritis, and on the right side evident traces of perimetritis and parametritis.

This patient returned fourteen months after her confinement, again in the pregnant condition. She was admitted to the hospital, and premature labor was brought on. During the labor elastic bags were employed to dilate the uterus, and strong labor pains were excited. It was determined to deliver the patient by Cæsarean section because of the danger of uterine rupture and the fact that labor did not proceed spontaneously. While she was being prepared for operation the heart sounds grew slower, and finally ceased, and

the patient's pains became much less and practically ceased. On opening the abdomen the breech and limbs of the child were found to have escaped from the uterus, while the head still remained within the cervix. The uterus had ruptured in its anterior wall near the site of the former rupture. The entire anterior wall was thin and dark in color through extravasated blood. The posterior wall was uninjured and of normal contour. The muscular tissue of the anterior portion of the cervix and lower uterine segment felt like ruptured elastic connective tissue. The uterus was so badly torn that it was impossible to recognize accurately the site of the former rupture. Hysterectomy was performed, and the stump drained by a strand of iodoform gauze passed into the vagina. The patient made a good recovery.

The opportunity was taken to examine the muscular tissue of the uterus microscopically to observe whether a degenerative process in the muscle was responsible for the rupture of the uterus. At the site of rupture the connective tissue of the uterus was infiltrated with blood, the capillaries much distended, the elastic fibres of the walls of the vessels distinctly demonstrable by staining, and individual muscle cells were found in a degenerative condition. There was no evidence of inflammation either recent or chronic, nor could any adequate explanation be found by microscopical examination for the repeated rupture and also for the location of the rupture.

The Formation of Decidua in the Fallopian Tube in Tubal and Intrauterine Pregnancy.—LANGE (*Monatschrift für Geburtshülfe und Gynäkologie*, Band xv., Heft 1, 1902) considers this question at length and gives the results which he has obtained in the examination of specimens from twenty cases. He has observed that just as in the gravid uterus there is the forming of a decidual membrane, so in the gravid tube to a less extent and with variable formation a decidua can exist. It is usual for decidua to form in the womb in most cases of tubal pregnancy. He finds that cases are reported showing that in tubal pregnancy decidua is formed in the non-pregnant tube and also in that portion of the uterus which is most adjacent to the tube. He examined a second series of five cases, and concludes from this investigation that the mucous membrane of the Fallopian tube, like that which lines the uterus, has the property of forming a decidual membrane. For this to happen the ovum must not only be in contact with the mucous membrane, but the impregnated ovum must form its attachment to the tube or to the uterus. The capacity of the mucous membrane of the tube for forming decidual membrane is much less than that of the lining membrane of the uterus. In the early months of pregnancy the tube forms scarcely any decidual lining membrane. Except in cases where the attachment of the ovum excites irritation in the tube during the early months of pregnancy, it is not uncommon to find the merest trace of decidual formation.

Three Cases of Cæsarean Section for Eclampsia.—In the *Centralblatt für Gynäkologie*, No. 5, 1902, LOWENSTEIN reports three Cæsarean sections for eclampsia.

The first was a primipara, twenty-eight years old, who had suffered during pregnancy from swollen legs and cough. She had a slow labor terminating in five eclamptic convulsions. The head was above the pelvic brim, the pelvis

was normal, the external os not dilated, and the membranes unruptured. Cæsarean section was at once performed, followed by the birth of a living child. A wide-spread bronchitis and nephritis supervened. Pneumonia followed, and the patient perished from respiratory failure. Autopsy showed purulent necrosis of the uterine cavity, with beginning peritonitis around the uterine stitches. There was stitch abscess in the abdominal wall.

Case second was also a primipara at full term, the fœtus in second position. She had had violent convulsions. The external os permitted the entrance of one finger, and the cervix was not shortened. She had no labor pains, and the child was living. An effort had been made to control the convulsions by morphia and chloroform without success. Cæsarean section was practised by transverse incision. The incision came down upon one corner of the placenta at the fundus. The uterus contracted well without much hemorrhage. The child was asphyxiated, but revived. The mother had a few slight convulsions after the operation. Immediately after the operation the patient seemed to improve, but later convulsions returned, and the patient perished from œdema of the lungs.

Case third was seven months pregnant and a primipara. She was unconscious, without pupillary reaction, when admitted to the hospital. Convulsions supervened, five occurring in two hours. The urine showed an excessive quantity of albumin. As hot baths and other remedies failed to control the convulsions, the child was delivered by Cæsarean section. The patient perished within the next twenty-four hours from rapid œdema of the lungs.

Embolus following Labor.—VOIGT (*Centralblatt für Gynäkologie*, No. 2, 1902) reports a case of central placenta prævia in which the placenta was perforated by the fingers, combined version made, and a foot brought down. A partially asphyxiated child was delivered shortly afterward. The uterus contracted well.

Three-quarters of an hour later the patient had a severe embolic attack with marked dyspnœa and rapid, feeble pulse. She gradually recovered during the nineteen hours following, but suffered from dyspnœa and weak action of the heart. Four days after labor a second attack occurred, with the formation of an infarct in the lung and bloody sputum. On the tenth day after labor a third attack happened and the patient expectorated blood with elastic lung fibre. The patient finally made a recovery in more than a month's time. He also reported two other cases, one after craniotomy, the second after spontaneous labor, in a weak and debilitated patient. Both of these patients recovered.

Death from Pressure of a Pregnant Uterus upon a Horseshoe Kidney.—WALSH (*British Medical Journal*, January 18, 1902) describes an interesting case recently reported by the coroner of the city of London. A young married woman died suddenly upon the street. Upon autopsy she was found several months advanced in pregnancy, and the enlarged uterus pressing upon a horseshoe kidney situated low in the abdominal cavity. Pressure had practically disorganized the kidney, and the sudden death was due to a resulting uræmia.

OPHTHALMOLOGY.

UNDER THE CHARGE OF

EDWARD JACKSON, A.M., M.D.,
OF DENVER,

AND

T. B. SCHNEIDEMAN, A.M., M.D.,
PROFESSOR OF DISEASES OF THE EYE IN THE PHILADELPHIA POLYCLINIC.

Diagnosis and Treatment of Glaucoma.—TERRIEN (*Le Prog. Méd.*, No. 34, 1901) observes that the etiology and pathogenesis of glaucoma are not yet understood. A single symptom is dominant from the clinical stand-point—hypertonus. Cases occur of excavation of the papilla without increased tension; it is doubtful whether these should be regarded as glaucomatous. According as the increase in the tension is sudden in an eye previously healthy, or takes place slowly and progressively, permitting the organ to accustom itself to the change, the symptoms will be those of acute and chronic glaucoma respectively. Chronic glaucoma is simple, if the increase in tension is slight and unaccompanied by appreciable changes, or irritative in the opposite case. Each of these three varieties requires special treatment.

(*a*) *Acute glaucoma*—sudden steps with intervening remissions: It is preceded usually by prodromic attacks. Suddenly after fatigue, or a heavy meal, or without appreciable cause, the vision is disturbed; objects appear smoky, lights are surrounded by rainbows. If the eye is examined at the time of the attack it will present the following diagnostic marks: 1. The pupil is slightly larger than that of the other eye, and reacts but slowly to light. 2. The cornea is somewhat hazy at its centre. This is the main cause of the disturbance of the vision. 3. The tension is increased. The prodromic attack lasts but a short time, several minutes or hours. After a variable period—days, weeks, or months—a second and third attack recurs; finally the intervals between the attacks become of short duration until an outbreak of acute glaucoma proper. The latter may occur at once without prodromes; if carefully sought for, however, the latter are rarely absent. It is important not to confound a prodromic attack of glaucoma with ophthalmic migraine. The symptoms of acute glaucoma are those of the prodromes very greatly accentuated. There is ciliary injection, extremely violent pains are present in the eye and the periorbital region radiating to the occiput. The pupil is dilated, a point which differentiates it from iritis. The anterior chamber is shallow. The small black pupillary margin of ciliary pigment reflected upon the anterior face of the iris, hardly visible in a normal condition, is more apparent. The tension is usually very high. Hybrid cases of iritis complicated with hypertonus (glaucomatous iritis) occur, and in these the diagnosis is different and has an element of danger in the possible use of atropine—a true specific in iritis, but which may entail the loss of the eye in glaucoma. The ophthalmoscopic examination is negative. The fundus cannot be illuminated, and the vision is *nil* or nearly so.

After a variable time, one to two weeks, all the symptoms diminish or disappear; the vision returns, though somewhat affected, and a slight degree of dilatation of the pupil persists. Attacks recur more frequently with incomplete remissions. The pupil remains dilated and the tension raised. The disease tends to become chronic, to terminate finally in blindness.

(*b*) *Chronic Irritative Glaucoma.* The beginning of the affection resembles the prodromic attacks of acute glaucoma; it is marked by transient obscurations with slight hypertonus. But the attacks and the remissions are less frank, and in the intervals the tension remains somewhat above the normal; thus a certain degree of tolerance of the organ is established. Apart from slight ciliary congestion and slight dilatation of the pupil, the hypertonus manifests itself only by changes in the fundus (dilated veins, arterial pulse, excavation of the papilla). It leads quite rapidly to blindness.

(*c*) *Simple Chronic Glaucoma.* Insidiousness is the essential characteristic. The tension is but slightly increased, and does not manifest itself by any external symptom. It betrays itself solely by changes in the fundus which may cause total excavation of the papilla and complete blindness without the patient being aware thereof, if the second eye remains healthy.

The importance of recognizing these three forms of glaucoma depends upon the fact that the treatment is very different for each form. They are not always sharply marked. Intermediate varieties occur following fluctuations in the degree of tension.

Treatment. This is both medical and surgical. The medical treatment consists entirely in the use of myotics combined or not with antiphlogistic measures (leeches to the temples, warm compresses, purgatives, etc.). Eserine, first employed by Laqueur in 1877, may be used in aqueous, or better, oleaginous solutions. The latter is more active, and the alkaloid is not transformed into rubreserine as in the aqueous solution. The strength should never exceed 1 per cent., whatever be the vehicle employed. Pilocarpine nitrate or salicylate is less energetic. It does not cause neuralgic pains. It is suitable for slight cases. The myotics in narrowing the pupil diminish tension, and this effect, the mechanism of which is little known, is very real. It is only palliative, never curative, and may be *nil* in certain cases. Under these circumstances it is necessary then to have recourse to surgical means, paracentesis, sclerotomy, iridectomy, etc. All these operations, requiring special skill and training, cannot be performed by every physician.

Acute Glaucoma. 1. At the beginning of the prodromic attacks myotics, combined with antiphlogistic treatment, may suffice to cause the attack to rapidly subside; the myotics should be employed in strong solutions—eserine in oil, or a mixture of eserine and pilocarpine. A recurrence is to be carefully watched for, and the patient or his family warned of the gravity of the disease and of the absolute necessity of preventing recurrence. During the attack instillations of eserine are to be employed morning, noon, and night. The effect of the myotics lasts but seven or eight hours. After the attack is over an instillation, morning and night, suffices, and the strength of the alkaloid is to be diminished. The myotic is to be kept up for a long time; indeed, it should never be entirely abandoned. An eye which has once suffered a single attack is predisposed to others, and it is rare that such do not occur. Myotics are, therefore, employed to put off such occurrence as

long as possible, and if a new prodromic attack does supervene it is to be treated as before, provided that the pupil becomes well contracted under the myotic and the attack rapidly disappears. Medical treatment is only to be employed in the beginning in the prodromic period, and on condition that the attack quickly yields to the myotics. The latter are to be continued in the interval between the attacks. But if the attacks are frequent and of long duration, the question of surgical intervention is to be considered. The operation may definitely arrest the progress of the affection. An iridectomy is the more efficacious the sooner it is done. But even then medical treatment is not to be neglected at the time of an attack; it will relieve pain, gain time until the arrival of the surgeon, and place the patient in better condition if an iridectomy is necessary. It cannot be sufficiently insisted upon that no mydriatic is ever to be employed in any form of glaucoma.

2. *Treatment of an Attack.* Iridectomy at once. No other choice is offered to the surgeon. Unquestionably the operation is not successful in all cases (about one-third), but it is the only measure which is successful in acute and subacute glaucoma. In chronic glaucoma the treatment is medical (see below). Iridectomy in glaucoma to be effective must be done early. We are still ignorant of the exact way by which the operation regulates the tension, but we can determine the anatomical conditions which must be present if iridectomy is to be successful in lowering tension and those in which the operation will be powerless. These conditions are to be looked for in the angle of the chamber. If it is obliterated the operation will be without effect. The iridectomy should be very wide, of keyhole shape, and before doing it myotics should be instilled into the eye. If the tension is very high and the anterior chamber obliterated a small sclerotomy should be done first, or, better still, scleral puncture with a Graefe knife, and the operation should be postponed until the next day or day after that when the anterior chamber is re-formed. It is only in this way that disasters can be avoided which may follow an iridectomy done upon an eye with excessive tension, luxation of the crystalline lens, grave intraocular hemorrhage, etc. Thus in absolute glaucoma the operation which may give good results, even under these circumstances, is only to be done with extreme prudence. Careful preliminary examinations should determine whether the glaucoma is of the hemorrhagic variety, in which case iridectomy must be rejected; or whether the absolute glaucoma is due to a tumor. In the first case arteriosclerosis is usually present. In the second the tension fluctuates greatly.

Done under these conditions iridectomy is capable of giving excellent results, definitely relieving the attack and preventing recurrences. After the operation the tension gradually becomes normal, the inflammatory symptoms yield, the sight returns to what it was before the attack, and the tension is little or not at all raised. But such an ideal result is not always obtained. In some cases the good effect is but slight. In others the disease progresses, or the iridectomy may even hasten the fatal process. This result is sometimes observed in chronic glaucoma, but very rarely in acute.

It is impossible to foresee, certainly, before operation, the effect of iridectomy, but there are certain points to be taken into account. The length of time the attack has lasted is of capital importance for the prognosis. If the iridectomy is done early, the first or second day after the beginning of the

attack, when the retina and papilla have not been exposed to the increased pressure long enough to be organically altered, diminution of tension, relief of pain, and re-establishment of vision may be hoped for. In the opposite case, especially where light perception and projection are faulty or absent, the prognosis must be very guarded. The operation may diminish tension and relieve pain but the vision remains compromised. The age of the patient is also of importance. Glaucoma is more serious in proportion to the age of the subject.

Iridectomy will not always prevent the return of new attacks. It is then necessary to open the old cicatrix or to make an incision in the sclera further back; these may give excellent results. If they fail, a second iridectomy is to be done opposite the first. In all cases myotics should be continued a long time (several months and even years). They should only be abandoned when it is certain that the disease has been definitely cured and shows no tendency to relapse. The effect of the myotic may at first sight appear doubtful, the sphincter of the iris being destroyed. It is, however, very real and capable of causing those slight and transient attacks of increased tension to disappear, which may occur after iridectomy—proof that the myotics do not act solely by contraction of the pupil. Iridectomy is the operation of selection in acute glaucoma. It should never be done, on the contrary, in hemorrhagic glaucoma and infantile glaucoma (buphthalmia), for which recourse must be had to less radical procedures (small sclerotomies, very narrow paracenteses, etc.); iridectomy in these cases may end in disaster.

3. *Chronic Irritative Glaucoma.* This form rarely constitutes a mean between acute and simple chronic glaucoma; iridectomy may be done at the time of the attack or in the intervals, especially if they recur frequently, the results are less certain. The operation is never so urgent; it may be replaced temporarily by sclerotomy or repeated paracenteses. According to the effect from these, it is possible to judge of what is to be expected from the iridectomy. Myotics are to be employed with or without surgical treatment.

4. *Simple Chronic Glaucoma.* The treatment is by myotics alone. Operation is without effect and may even be injurious. The myotics must be used for a long time and very regularly, three times daily. Pilocarpine nitrate, 1 to 50, suffices in mild cases; severe forms require eserine. Very narrow paracenteses and small sclerotomies are, as a rule, the only operative procedures permissible. The degree of tension furnishes an indication; if this is at all pronounced the prognosis is more favorable; surgical intervention may effect real improvement. M. Dianoux proposes sclerotomy with the massage. The evening of the operation gentle pressure is made upon the globe by the index fingers, alternating as in testing the tension, in order to separate the lips of the wound and determine partial evacuation of the aqueous humor; the manipulation is repeated morning and evening for five or six days, and the patient is taught to do it himself. Myotics are instilled into the eye for a long time; quinine and iodide of potassium are given internally. Finally, if the disease continues to progress, section of the sympathetic is justifiable. This operation is of too recent date to be judged definitely. The results seem to be but little encouraging. Improvement, even if it occur, is never permanent.

Etiology and Treatment of Convergent Squint.—WORTH (*Lancet*, May 11, 1901) presents conclusions based on 1278 personal cases. Squint is not simply a deviation of the visual axis of one eye as defined in the text-books. In addition to the deformity there are four other elements. 1. Deficient development of the fusion faculty. 2. Suppression of the image of the deviating eye. 3. Amblyopia usually. 4. Refractive error. Squint is not a muscular defect In over 83 per cent., outward rotation of each eye was normal. In 9 per cent. abduction was defective in each eye, and in only 7.7 per cent. the defect was confined to the deviating eye. In constant squint the zero of convergence is some cross-eyed position, instead of parallelism. Of constant squint, 89 per cent. are monolateral, and 11 per cent. alternating. In 809 of the 1278 cases the age at which the deviation appeared is as follows: Before one year of age 102 cases, about 12 per cent.; between one and two years, 142 cases, about 17.5 per cent.; between two and three years, 195 cases, about 24.5 per cent.; between three and four years, 159 cases, about 19.5 per cent.; between four and five years, 91 cases, about 11 per cent.; between five and six years, 58 cases, about 7 per cent.; after six years of age 62 cases, 7.5 per cent. Thus, in 74 per cent. the deviation appeared before the end of the fourth year; and in only 7.5 per cent. was it delayed until after the end of the sixth year. At the first appearance of a monolateral squint there is often a considerable degree of congenital amblyopia in the deviating eye, and occasionally in the other eye also; but the deviating eye always first has the power of fixation when the other is covered. If the case is not properly treated the deviating eye becomes blinder from disuse. After a time in a considerable proportion of cases the deviating eye loses the power of central fixation. This loss is especially likely to occur in young squinters; so that there is a wide-spread belief that an eye which deviates during the first twelve months of life is very blind; yet this is not the case. Thirty per cent. treated by glasses alone eventually become straight—the spurious squint of infants. Ocular co-ordination is very rudimentary during the first few months of life. It often happens that the eyes momentarily deviate. This is of no importance. If, however, true squint be present, treatment is demanded without delay.

Etiology. The essential cause of squint is a defective fusion faculty. All other causes are but predisposing—hyperopia, anisometropia, congenital amblyopia. Heredity is a very strong predisposing cause. In 1028 cases there was a history of squint in father, mother, brother, or sister in 51 per cent.

Treatment. The indications are four: First, to prevent the loss of central fixation; second, to prevent deterioration of vision; third, to train the fusion faculty; fourth, to restore the visual axes to their normal directions.

Full correction of the refractive error is to be prescribed as early as possible, even under twelve months (?). To exercise the deviating eye atropine is dropped into the straight eye. The common practice of dropping atropine into both eyes is wrong. Neglected cases with acquired amblyopia or loss of central fixation are usually quite hopeless. The author's amblyoscope is adapted for squint of any degree. Suppression of the image is overcome by unequal illumination of the object slides. The variety of the pictures amuse and interest the child.

Operation. If binocular vision cannot be obtained, operation is to be deferred to the age of eight or nine years. If the amblyoscope has produced a strong desire for fusion, operation may be performed at any age. Operation is indicated when periodic measurements of the angle of squint shows that this is either not decreasing or decreasing very slowly. The dynamic convergence should always be examined. If the fixing eye suddenly fixes a nearer object, a dynamic convergence is superadded to the abnormal static convergence. If the dynamic convergence is very deficient, simple tenotomy is strongly contraindicated. If the fusion faculty has been developed and binocular vision is expected after operation, a tenotomy is never done except in combination with an advancement. The author maintains that the great cause of failure in advancement is the difficulty of getting the sutures which pass through the muscles to hold. The tough fibrous tissue at the margin of the cornea furnishes a suitable anchorage.

Ophthalmic Complications of Plague.—MAYNARD (*British Medical Journal*, September 14, 1901) reports twelve cases during the recent epidemic in Patna, India. Six recovered with one eye sound. In the eighteen eyes the following lesions were noted: Cornea, hazy in four, opaque in two, and sloughed in four; iris, iritis in twelve cases from the mildest to occlusion pupillæ; sclera, staphyloma in two; lens, hazy in seven and quite opaque in five. The media were hazy in six; the fundi showed hemorrhages in one. The tension was diminished in twelve cases. Vision *nil* in five, light perception in eight, and fairly good in five.

DERMATOLOGY.

UNDER THE CHARGE OF

LOUIS A. DUHRING, M.D.,

PROFESSOR OF DERMATOLOGY IN THE UNIVERSITY OF PENNSYLVANIA,

AND

MILTON B. HARTZELL, M.D.,

INSTRUCTOR IN DERMATOLOGY IN THE UNIVERSITY OF PENNSYLVANIA.

Multiple Nodular Melanocarcinoma of the Skin from a Nævus.—A. RAVOGLI (*Journal of Cutaneous and Genito-Urinary Diseases*, June, 1901) describes the case of a married woman, aged thirty-three years, the mother of two children, who from birth had a pigmented nævus verrucosus, the size of a silver quarter-dollar, in the middle of the sternal region. At the age of thirty-one years, while pregnant with her second child, it first began to grow. It was excised. Two months later numerous disseminated, dark-brown nodules appeared around the scar and for a considerable distance away from it, accompanied by painful itching sensations, preventing sleeping.

Microscopical examinations of excised nodules were made, and a question of interest was whether the disease should be regarded as being sarcoma or carcinoma. Clinically, the growth looked like sarcoma, but the microscope made the diagnosis of carcinoma certain, thus confirming the views and the doctrine of Unna on this important subject. The author thinks that cases of this kind are identical with those designated in olden times as *noli me tangere*.

Eruptions Due to Orthoform.—W. DUBREUILH (*La Presse Médicale*, May 18, 1901) states that while it is generally admitted that this drug is innocuous and is usually well tolerated, the fact that it is sometimes productive of eruptions should be kept in mind in prescribing it. The eruptions in the skin, when they occur, are usually (1) erythematous, complicated or not by vesiculation or pustulation; or (2) ulcerative and gangrenous. Two typical instances of the latter variety are given, both in women, one involving the anal and genital region, the other the hands, the lesions being both ulcerative and gangrenous. The author calls attention in particular to the observation, not heretofore noted, that the analgesic property of the drug persists upon the lesions which it itself has produced upon the skin.

Chaulmoogra Oil Subcutaneously Injected in Lepra.—DU CASTEL (*La Semaine Médicale*, March 6, 1901) reports the results of treatment according to this method in four cases, with the dose of seventy-five grains daily. In general, the injections benefited the leprous lesions, especially those of ulcero-tuberculous form; but they always gave rise to severe pain and often to inflamed nodes, and occasionally to grave fatty embolism, so that this method of treatment should only be employed in very rebellious cases, and never in the arms (as advised by Tourtoulis Bey), but only in the subcutaneous cellular tissue of the thighs or abdominal walls.

Crude Petroleum of No Value in Baldness.—G. T. JACKSON (*Journal of Cutaneous and Genito-Urinary Diseases*, June, 1901) is to be commended for the frankness with which he discusses the value of remedies. In the case of crude petroleum he found that no good results followed its local application for a period of from three to seven months, tried in a number of patients affected with baldness. The disagreeable odor of crude petroleum may in part be overcome by using a mixture of one part of cologne water and two parts of the oil.

Action of Concentrated Light on the Skin as a Therapeutic Agent.—A. RAVOGLI (*Journal of Cutaneous and Genito-Urinary Diseases*, December, 1901) gives his experience in the treatment of several cases of lupus vulgaris and lupus erythematosus, in all of which it was beneficial and in some very satisfactory. The apparatus employed was that made in accordance with Finsen's principles as modified by Lortet and Genoud, of Lyons. It consists of an arc light, the rays passing through a small condenser. In this way the force of the heat rays are diminished, which are absorbed by nearly any medium in the condenser. The lenses are of quartz, and water circulates in them and in the shield which contains the light, so that the apparatus is

perfectly cool; thus the heat rays are prevented from going through, without any obstacle to the passage of the chemical rays. The photochemical intensity is so strong that a ten to twenty minutes' exposure is sufficient. The method of treatment is based exclusively on the application of the chemical rays, blue, violet, and ultra-violet. The physiological action of the treatment consists of a local erythema, sometimes followed by the formation of vesicles, ending in six or eight days in epidermic exfoliation; followed by diminished congestion and re-absorption. Hypertrophic lupus nodules become flat, small, and in the middle show a kind of necrotic appearance, and then disappear. The effect on ulcers is admirable. According to the size of the lesion, large or small lenses are employed. Reference is made to Finsen's now well-known work and to his satisfactory results therapeutically.

The Histopathology of Lupus Erythematosus and of the Elastic Fibres.—P. H. SCHOONHEAD (*Archiv für Dermatologie und Syph.*, Bd. liv. p. 163) excised skin in 11 cases of this disease, and examined the same after preparation in alcohol, formol, Müller's and Flemming's solutions, and staining with various methods. He concludes that in the beginning the inflammatory process attacks the reticular portion of the skin, and that the sebaceous and sweat glands are involved in the earliest stage. Later the connective tissue undergoes hypertrophy, the areas of infiltration, formerly circumscribed, become more diffused, and the epithelial layers assume a distinct tendency toward keratinization. When the progressive changes come to an end marked degenerative changes occur in the elastic fibres, and it is these changes that cause the peculiar scar-like atrophy so characteristic of the latter stages of the disease. This atrophy takes place in the upper strata of the corium, and herein lies the explanation of the scars being so superficial and soft. The author considers that the disease has such distinctive histological features as to entitle it to a place distinct from all other diseases of the skin.

The So-called Angioneuroses of the Skin.—L. TOEROEK (*Archiv für Dermatologie und Syph.*, Bd. liii. p. 243) considers that writers have committed an error in their interpretation and acceptance of the cutaneous angioneuroses. From a review of the various well-known authors (especially German) and his own observations, he concludes that all the symptoms which serve as a basis for considering certain pathological changes in the skin as due to an angioneurosis and to an inflammatory process cannot be regarded as such; and that the cutaneous manifestations of urticaria, erythema multiforme, and erythema nodosum cannot be looked upon as simple "inflammations."

Parakeratosis Variegata.—T. COLCOTT FOX and J. M. H. MACLEOD (*British Journal of Dermatology*, September, 1901) report a new case of this rare dermatosis, the first observed in London. The patient was a healthy adult male with a good family and personal history. At the age of thirty-one a circumscribed red patch, covered with fine scales, appeared in the lumbar region, unattended by subjective symptoms, except cracking on bending. About the same time the palms became thickened and the sense

of touch dulled. In six months the patient was covered all over except the face with a hard, dry skin. The scalp was scurvy, the hair falling out to some extent, but the nails were healthy. This condition of the skin persisted, in spite of various forms of treatment, for five years without change. The efflorescence consisted of a hyperæmic mottling in the form of a network, the threads of which were made up of macules and slightly raised, scaly papules. There was hyperkeratosis of the palms, and, to a less extent, of the soles. The author's conclusions from a study of this case and those reported by other observers are as follows: Parakeratosis variegata is a clinical entity. It attacks chiefly the male sex, usually occurs in adult life, and the patients are generally in robust health when attacked. We know little of its etiology, but its general configuration and histology suggest a vasomotor disturbance associated with œdema and infiltration of cells in the corium and secondary changes in the epidermis. The initial lesion is a macule, or maculo-papule of small size, flat on the surface, and covered with a fine, adherent scale, which may be scratched off without causing bleeding. By the coalescence of the lesions a peculiar retiform arrangement results, in which areas of normal skin are enclosed, and which, combined with differences in the color of the lesions in the more dependent parts of the body, produces the marbled or variegated appearance of the dermatitis. It affects the skin almost universally, except, as a rule, the face, scalp, palms, and soles. It is subject to remissions and exacerbations, but is peculiarly chronic in its course. Marked subjective symptoms are absent; and it is resistant to local treatment. It consists histologically of a superficial inflammation affecting the subepidermal layer, with dilatation of vessels, œdema, and infiltration of cells, and an œdematous condition of the epidermis with more or less defect in the process of cornification. It may be regarded as belonging to a group of superficial inflammations of the corium, with secondary changes in the epidermis, which the authors have provisionally called "Resistant Maculo-Papular Scaly Erythrodermias."

Lepra.—Victor Babes (*Journal of Cutaneous and Genito-Urinary Diseases*, December, 1901, p. 576), the well-known pathologist and clinician, contributes a valuable book on this disease, chiefly the result of personal experience. He is a firm believer of the contagiousness of the disease, and substantiates his views with impressive observations obtained in his native land, where lepra is prevalent. He regards external unfavorable conditions such as climate and diet as favoring, but not as producing, the disease. Neither does he regard the disease as hereditary. When the children born of leprous parents are removed from their surroundings they rarely become lepers. The bacillus of lepra up to the present date has not been successfully cultivated. It is allied to the tubercle bacillus—the general and local reaction of leprous individuals when tuberculin is injected into them seems to confirm this view. The chief prophylactic remedy is seclusion and governmental supervision, the establishment of lepra districts and colonies where the disease is prevalent.

Acetanilid-iodized Starch Powder as a Local Remedy.—T. G. Lusk (*Journal of Cutaneous and Genito-Urinary Diseases*, December, 1901) speaks

highly of the value of the following combination in numerous diseases, applied in the form of a powder or a paste: Acetanilid, ʒj; zinc oxide, ʒiij; iodized starch, 5 per cent. ʒiv. It is necessary that the iodized starch be properly prepared and the acetanilid finely pulverized. Sufficient water is added to make a paint or paste, to be applied with a stiff brush. Liquid albolene, benzoin or olive oil may be used instead of water when the application is intended for dry surfaces or ulcers; a gauze bandage may be used to prevent it from being rubbed off. When dry the powder is of a light drab color, when wet of a slate color, but when in contact with pus it turns white, showing that the iodine has been liberated. This combination of the drugs gives an antiseptic, astringent, soothing, and protective remedy, having remarkable healing properties, useful in eczema, ulcers, dermatitis from all causes, including superficial burns, impetigo sycosis, herpes zoster, and chancroids.

HYGIENE AND PUBLIC HEALTH.

UNDER THE CHARGE OF

CHARLES HARRINGTON, M.D.,
ASSISTANT PROFESSOR OF HYGIENE, HARVARD MEDICAL SCHOOL,
AND
EDWARD F. WILLOUGHBY, M.D.,
OF LONDON.

Bacterial Contamination of Milk.—In order to determine the degree to which milk is necessarily contaminated during milking, and the extent of bacterial growth which occurs during transit from the dairy to the city, DR. W. H. PARK, of New York (*Journal of Hygiene*, July, 1901, p. 391), undertook a series of investigations which yielded most striking and important results, which indicate that milk with far less bacterial contamination than is commonly the case can be supplied without appreciable increase of expense to the farmer and shipper. The milk of large cities comes necessarily from a wide extent of country, and part of it at least is, on arrival, already from twenty-four to forty-eight hours old, during which time the original bacterial content has enormously increased. Of the influences which determine the number of bacteria in the milk of healthy cows, cleanliness in procuring, the degree to which it is cooled, and the length of time it is kept can be almost completely controlled. Reference is made to the inexcusable lack of cleanliness in the methods of procuring milk and of care in cooling and keeping it during transportation, and to the unnecessary delay in shipping.

Milk obtained from cows where every reasonable means was taken to insure cleanliness, cooled within an hour to 45° F., and subsequently kept at that temperature, yielded after forty-eight hours an average of less than 11,000 bacteria per cubic centimetre. Taken during winter in well-ventilated, fairly clean but dusty barns, and cooled within two hours to 45° F., the visible dirt having been cleaned off the hair of the udder; the milker's

hands having been wiped off, but not washed; the milk pails and cans being clean, but the straining cloths dusty, it averaged after forty-eight hours 75,000 bacteria per cubic centimetre. Taken from more or less dirty cows stalled in ordinary barns, the teats having been cleaned slightly in the usual way by running the unwashed hands over them once before milking, it averaged after forty-eight hours in winter and in warm weather, respectively, 210,000 and 680,000 bacteria per cubic centimetre. Twenty samples of ordinary city milk taken immediately on arrival, many of them having been transported over 200 miles, yielded from 52,000 to 35,200,000 bacteria per cubic centimetre. Milk as sold in the shops yielded the following average figures: From the poorer tenement districts in midwinter, 1,977,692; in September, 15,163,600. From the more well-to-do districts in midwinter, 327,500; in September, 1,061,400. The influence of temperature was well shown by the results obtained on allowing portions of the same specimen to stand at different temperatures. Kept for twenty-four hours at temperatures below 50° F., no marked change occurred in the number of bacteria (3000) originally present per cubic centimetre, but at higher temperatures most astonishing growths occurred. Thus, at 60° F., 180,000; at 68° F., 450,000; at 86° F., 1,400,000,000, and at 94° F., no less than 25,000,000,000 per cubic centimetre. At the end of forty-eight hours, the specimen kept at 60° F. had increased its bacterial content from 180,000 to 28,000,000, and that at 68° F. from 450,000 to 25,000,000,000. Those kept at the lower temperatures had not materially changed.

Park concludes that the most deleterious changes which occur in milk are not those due to ordinary adulteration, but are those produced by the multiplication of bacteria, and holds that it is the duty of health authorities to prevent the sale of milk rendered unfit for use through the bacteria and their products, and to force gradually the farmers and middlemen to use cleanliness, cold, and despatch in the handling of their milk. As to standards, he believes in beginning with one of 500,000 for milk on entrance and 1,000,000 on delivery. These figures are conceded to be ten times as high as milk should show, but by the enforcement of such a standard the farmer would receive a compulsory education in the necessity of preventing the presence and multiplication of bacteria.

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All communications should be addressed to

DR. FRANCIS R. PACKARD, 1831 Chestnut Street, Philadelphia, U. S. A.